A HANDBOOK OF TROPICAL DISEASES

A HANDBOOK OF
TROPICAL DISEASES

WITH TREATMENT AND PRESCRIPTIONS

BY

J C BANERJEA

M B (CAL) M R C P (LOND)

P f f M d cine M d l C ll g C l t

AND

P B BHATTACHARYA

M B D T M (CAL)

Lat Tea l f M d ci R ldshay M d l School B rd e W B g l

SIXTH EDITION

Th ghly ew ed d d d w th th f

L K GANGULI

B SC M D (CAL) M R C P (EDIN) MAJOR A M C /Res

D p rtm t f M d N lrat S M d l C ll g C l tt

d th trib t by

R N CHAUDHURI

D t nd P f f T p l M d S hool f Trop l M d C tt

N V BHADURI

L t H d f th D partm t f H lm th l gy d F la S hool f T p cal M d C l tt M mb S th P ef C mm F l n n

P C SEN GUPTA

P f f P th l gy d Cyt l gy S h l f T p cal M d ci C l tt

A MONDAL

S p n t d t f f t Di H p t l C l tt

L K GANGULI

Hony V nt g Phy ci N b t S ca M d l C ll g H p t l C l tta

J B CHATTERJEA

Prof f H m t l gy School f T pical M d ci C l tt

ACADEMIC PUBLISHERS CALCUTTA

1960

PREFACE TO THE SIXTH EDITION

Since the publication of the Fifth Edition in 1952 a good amount of new materials has piled up and much rapid advances have been made in the field of drug therapy. To incorporate them in an easily understandable and condensed form without altering the clinical character of the book, it was felt that the task would be formidable without the help of contributors.

We have been able to enlist the help of a group of contributors who are connected with both under graduate and post graduate teachings in Tropical Medicine for a long time. With their help it has been possible to review the respective sections completely and add new chapters on Giardiasis and Tropical Eosinophilia. Our sincere thanks are due to them for their effort to make this edition an improvement upon all the previous ones.

Certain basic changes have been made in the presentation to which we wish to draw attention. As amoebiasis at present happens to be the commonest problem we thought it best to begin with this disease as the first one instead of malaria. Blackwater fever has not been considered a separate disease entity and so has been dealt with in the same chapter as malaria. Kala azar, dermal leishmanoid and oriental sore now have been grouped under leishmaniasis. The nomenclatures ancylostomiasis and oxyuriasis are changed. In the case of the former the term hookworm disease has been used as the main causative organism of the disease in India is *N. americanus* and not *A. duodenale*. Typhus fevers have been put under a new section Diseases caused by Rickettsias. Epidemic dropsy, snake bite and scorpion sting have been grouped under one section Diseases caused by Poisons. Tropical splenomegaly has been shifted under Diseases of Unknown Aetiology.

It has been our experience that materials presented on the diagnosis of fevers and diarrhoeas in the tropics and the therapeutic guide containing useful prescriptions are of immense help to the students. We therefore retain them. A major departure from the usual custom is the presentation of index. Separate indices for the subject matter and drugs have been prepared. We hope that this change will be helpful to both the students and practitioners.

Illustrations of the previous editions have been completely replaced by new and appropriate ones. The coloured plate showing the various

erythrocytic stages of development of malaria parasites have been prepared after Beyer's *Microscopic Diagnosis of Tropical Diseases*. In the description of the diseases we have tried our best to keep to a particular form. Alterations in some are due to the express wish of the particular contributor.

We acknowledge our indebtedness to Dr. L. K. Ganguli without whose assistance it would not have been possible to edit, illustrate and bring the book up to date. The credit of preparing the drug index and going through the proofs also goes to him.

We thank the Academic Publishers and Sri T. Basu, the printer, for their active co-operation and help.

Lastly, we hope that the present edition of the Handbook will continue to prove instructive and helpful to the students and the practitioners. The authors are grateful for the criticisms and suggestions for the improvement of the book in the past and look forward for them again.

J. C. BANERJEA
P. B. BHATTACHARYA

Calcutta
21st July, 1960

PREFACE TO THE SECOND EDITION

Encouraged by the enthusiasm with which the first edition of the Handbook of Tropical Diseases was received by the medical students and general medical practitioners we have brought out this second edition which is largely re-written, enlarged, thoroughly revised and up-to-date.

The contents of this volume have been divided into thirty one chapters supplemented with an Appendix and an Index. The various chapters have been grouped on an etiological basis under nine sections which include new articles on Dermal Leishmanoid, Oriental Sore, Typhoid and Paratyphoid Fever, Chickenpox, Typhus Fever, Rabies, Rat bite Fever, Relapsing Fever, Helminthic Diseases such as Taeniasis, Acariasis, Trichiniasis, Trichuriasis and Oxyuriasis, Snake-poisoning, Scorpion bite and Heat Stroke comprising Heat Hyperpyrexia, Heat Exhaustion and Heat Cramp. The chapters on Dysentery, Cholera, Plague, Leprosy, Smallpox, Dengue, Ancylostomiasis, Filariasis, Sprue, Beriberi and Epidemic Dropsy have been entirely re-written. Those on Malaria, Blackwater Fever and Kala-azar have been thoroughly re-arranged and partly re-written. In the consideration of the diseases we have endeavoured to present a clear and concise account of their aetiology, pathology, clinical manifestations, diagnosis, differential diagnosis, prognosis and treatment. All unnecessary theoretical details have been deliberately avoided and much useful practical hints, especially on methods of diagnosis and treatment have been incorporated.

The Appendix consists of two portions, the first of which deals with the diagnosis of fevers and diarrhoeas in the tropics, whereas the latter portion includes a list of well-chosen prescriptions which we hope will prove very useful to the busy young medical practitioners.

Many illustrations and coloured plates have been added to this edition and their source has been duly acknowledged. The coloured plates on the microscopic appearances of the stools in amoebic and bacillary dysentery have been reproduced from Knowles's Protozoology.

These additions and alterations have therefore necessitated an appreciable increase in the size of the book.

In the compilation of the book we have, as in the first edition, frequently referred to the various existing standard text-books on

SECTION IV DISEASES CAUSED BY SPIROCHÆTES

SECTION V DISEASES CAUSED BY RICKETTSIÆ

SECTION VI DISEASES CAUSED BY VIRUSES

SECTION VII DISEASES DUE TO VITAMIN DEFICIENCY

SECTION VIII DISEASES CAUSED BY POISONS

Subsection A Vegetable Poisons

Subsection B Animal Poisons

SECTION IX DISEASES DUE TO PHYSICAL AGENTS

SECTION X DISEASES OF UNKNOWN ÆTIOLOGY

Appendix

Index

A HANDBOOK OF TROPICAL DISEASES

SECTION I

INTRODUCTION

Geographically tropical means the area bounded by the Tropic of Cancer and the Tropic of Capricorn It is natural therefore to expect that the word tropical should be related and applicable to those specific diseases which are only tropical in distribution that is the diseases are associated with tropical climate which is encountered in a zone extending from the Equator to the area where the mean annual isotherm is 20°C (68 F) Thus on the basis of isotherm the area includes Central America a large portion of South America and Africa Madagascar the West Indies a portion of India Ceylon Arabia Indo-China Sumatra Java Borneo the Philippine Islands New Guinea a part of Australia and a number of small islands

At the very outset it is imperative and essential to make it perfectly clear that any present day discussion on tropical disease does not mean that it is related to the climate or the geographic area

The so called tropical diseases are not limited to the tropics only but are also prevalent in the temperate zones There are various other medical conditions which occur in the tropics in common with other non tropical regions of the world

How then the label tropical diseases has come into being with the establishment of what modern tropical medicine is today?

In the early times medicine was relatively highly developed in the East (Egypt and India) while it was very primitive in the West The West however was aware of the existence of the East The problem of finding a way to the East was solved in 1415 A D and in the last decade of the fifteenth century the route to India via Cape was made known The urge to discover new lands heightened and regular channels of trade and commerce were established the travel being at that time limited to overland and sea routes The latter was much preferred and thus meant more ships and numerous crews To keep the crews fit during the course of long journeys it was customary to provide a surgeon or a person with medical knowledge for each vessel Many of them were not only intelligent but had great powers of observation also Out of them some settled in these new lands and made records of their experiences In this way a curious collection

of facts developed based partly on geography partly on zoology and botany partly on ethnology and partly on medicine And in these early collections are found references to the diseases prevalent in the tropics and perhaps thus sprang the words *tropical diseases and medicine*

With the increase in settlements founded by Europeans and their families the number of medical practitioners also increased Newer knowledge and newer diseases unknown in temperate zones soon resulted in numerous publications This naturally reflected on the teaching and Tropical Disease and Tropical Medicine became a eparate unit out of medicine as a whole

In the course of the last few centuries the pattern and the incidence of many diseases have altered History has shown that the diseases which were once cosmopolitan maladies occurring endemically or in epidemics are more prevalent and getting increasingly confined to the tropics at present Complete eradication of such diseases from the most part of the temperate zones has not been the result of climatic influence but because of stricter methods of isolation preventive measure improvement in economic status better sanitation and hygiene and better nutrition that is through achievement of positive health

There are no feasible grounds to support the idea that there ought to exist a special category of diseases which are to be classed as tropical diseases What diseases therefore should or ought to be considered as tropical? It appears that to start with only certain diseases which were commonly encountered by settlers in the tropics only were thought to be tropical With betterment of communication and with easier and faster travel facilities dissemination of tropical diseases became quicker and widespread Thus at present separation of tropical medicine from *body corporate of medical sciences is artificial The present day* categorisation is therefore based more on tradition and arbitrary selection than logic There are only a very few diseases which do not occur in the tropics and there are many which are as common or commoner in the temperate zones Perhaps diseases which are more prevalent in the tropics and exhibit special features ought to be classed as tropical diseases Even so the changing face of the disease incidence will be a bar in accepting the contention in toto One of the living examples is the rapid decline and extinction of malaria the notorious killer from many of the tropical regions The other difficulty is that the diseases in the tropics show marked variation in their incidence from place to place and from season to season

Transmission of tropical diseases is seldom simple or straight forward for there is not only the parasite itself to be considered but

the presence of an insect vector an intermediate host and an animal reservoir has also to be taken into account The geographic distribution of some of the tropical diseases is linked with the presence of proved vectors The incidence therefore varies according to the distribution of these insect vectors Many of the insects infest habitations specially the slums and rural areas Some of them are merely mechanical transmitters contaminating food and drink by physical contact only Many however bite and cause serious and fatal diseases Moreover because of the heat major part of the body is usually kept bare and thus is the ideal target for the biting insects

Water is another chief source of the diseases in the tropics Bathing is a daily necessity Water is also used from a common source for drinking laundering and ablutions Fæcal contamination is a constant source of infection

Another factor which makes the people of tropical countries more vulnerable to disease is the lack of balanced diet particularly the lack of animal proteins which are beyond the reach of the majority Low economic condition and non availability of pure food predispose the people to more nutritional disorders Majority suffer from subclinical deficiency state

This handbook deals with the so called tropical diseases on the basis of tradition Moreover in this book have been included only those diseases which are commonly prevalent in India only Thus yellow fever and sleeping sickness though typical examples of tropical diseases have not found a place

Malaria is no longer the most important disease in India at present There are only pockets here and there and it is expected that within a few years to come the disease will be completely wiped out Visceral leishmaniasis now occurs in sporadic manner in the Gangetic plains of Bihar and West Bengal Cutaneous variety is still prevalent in the drier Northern and Western plains of India

The incidence of bowel diseases is at present a major problem and yet to be controlled Amœbiasis now tops the list of all the tropical diseases and at present is more or less endemic throughout India Cholera still occurs as epidemic in the State of West Bengal Enteric fevers bacillary and flagellate diarrhœas still occur endemically Supply of safe drinking water and adequate facilities of purification do not exist even in cities

The alarming increase of leprosy in the low lying hot and humid areas of West Bengal Orissa and the Eastern parts of South India is assuming a major problem

Regarding helminthic infestations hookworm disease is the most common and harmful infection prevalent throughout India The infection is almost solely due to *N americanus* The incidence of filariasis is also on the increase particularly so in the whole of the Southern part of India and in the States of Orissa and West Bengal

Since the World War II and the partition of India the nutritional status of the people of India as a whole has fallen far short of the standard Few can afford the required intake of proteins and whatever food is available is also adulterated Use of fruits happens to be a luxury Consumption of milk is negligible because of non availability and high cost Nutritional diseases are therefore on the increase

The ætiology of tropical splenomegaly still remains a problem Recently one more serious condition tropical eosinophilia has risen into prominence With its pulmonary manifestations and relapses it is one of the most debilitating diseases

Incidence persistence and spread of tropical diseases in India are influenced by rainfall in the locality nature of water supply terrain and environments These are far more important factors in the tropics than in the temperate zones

More often the incidence is dominated by human factors *Melas* pilgrimages and religious gatherings taking place all the year round and occasionally with special significance at intervals are the prime factors Unhygienic social conditions apathy in the achievement of positive health ignorance prejudices and poor economic status all add to predisposition not only to tropical diseases but to every other disease prevalent in the tropics

The physical geography during the last few thousand years has not much changed The changes in the flora and fauna are also not considerable Whatever change has occurred it has taken place in the social and economic status

All tropical diseases to day are preventible and in most cases curable The tropical diseases when reduced to fundamentals are related to three main factors water supply insect vectors and food The role of climate has rather been exaggerated in the textbooks of tropical medicine in the past Residence in tropical climate means nothing but physiological adjustment to heat light and humidity

The word *Tropical* perhaps from the point of view of medical sciences does not mean the geographical region or the climate but the living conditions and sanitary standards

L K G

SECTION II DISEASES CAUSED BY PARASITES

SUBSECTION A PROTOZOAL DISEASES

CHAPTER I

AMŒBIASIS

DEFINITION

It is an infection caused by the protozoan *Entamœba histolytica* Involvement of the large intestine producing dysenteric signs and symptoms is known as amœbic dysentery The term amœbiasis therefore includes not only the involvement of the colon but also involvement of other organs of the body

HISTORY

Differentiation of dysenteries before 1875 was not possible It was Losch (1875) who first reported the findings of amœbae in the stool of dysenteric patients In 1903 Schaudin first pointed out that *E histolytica* is the causative organism of dysentery During World War I Dobell (1917) and other workers made extensive studies in the nature and pathogenesity of *E histolytica*

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It has a world wide distribution It is prevalent as a major bowel disease in the tropics and subtropics It is very common in India The overall incidence in W Bengal is about 30 per cent

Amœbic dysentery occurs frequently in sporadic forms than epidemic ones There is no particular seasonal prevalence It is frequently common in families and dormitories Sewage polluted water food handled by cyst passers and the house flies are the common and main factor in the spread of the disease

AGE AND SEX INCIDENCE The disease may occur at any age It is rare in young children under five years due to a lesser chance of exposure to infection Both sexes are equally liable

CAUSATIVE ORGANISM *E histolytica* the causative organism exists as trophozoitic or vegetative forms and precystic and cystic forms

Trophozoitic or Vegetative Form The vegetative form in living condition measures about 20 30 μ about three times the diameter of

a R.B C *It is a clear slightly greenish transparent body having a finely granular endoplasm surrounded by a clear and thin ectoplasm* It has a characteristic active movement effected by *protrusion of clear* pseudopodia. The shape is therefore ever changing The endoplasm contains a fine delicate ringlike nucleus and varying number of ingested corpuscles (Fig 1) which is an important diagnostic feature. The vegetative forms lose their power of movement and die very quickly within two hours after the passing of the stool

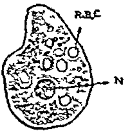


FIG 1 *Entamoeba histolytica* —Vegetative stage [N—nucleus]

Precystic and Cystic Forms The vegetative forms of *E histolytica* enter the precystic stage which is smaller than the ordinary forms and then begin to encyst under conditions adverse to their living and multiplication and pass out with the faeces The cysts are much smaller than vegetative and precystic forms vary much in size from 7 to 15 *microns* in diameter and have got a distinct cyst wall. The shape is usually round and may be oval They contain masses of chromatin bodies and vacuoles con



FIG. 2 *Entamoeba histolytica*—Cystic stage
1—Mono-nucleate 2—Bi nucleate 3—Tetra nucleate.
[N—nucleus C—chromatin bodies]

taining glycogen (Fig 2) In the early stage they contain one nucleus [Fig 2 (1)] which divides and multiplies when mature each of them contains 4 small nuclei [Fig 2 (3)] and very little glycogen which is used up Most of the cysts degenerate slowly in the passed stool Mature tetra nucleate cysts are relatively resistant. Mature cysts can live for 2 to 3 weeks or even more if kept moist and cool Desiccation kills them rapidly

MODE OF INFECTION

Contamination of food and drink by the *E histolytica* cysts is the most important factor in the spread of the infection from man to man Such a contamination may occur in the following ways

1 HUMAN CARRIERS Human carriers passing cysts of *E histolytica* in their stools are chiefly responsible for the occurrence and the spread of the disease Carriers may be of two types

(*a*) *Contact carriers* who have never suffered from amœbic dysentery

(*b*) *Convalescent carriers* who have previously suffered from acute amœbic dysentery or diarrhœa and have not been completely cured

Such persons when entrusted with the preparation and distribution of food and drink are the most frequent and common sources of infection

2 INFECTED WATER SUPPLY Infection occurs by swallowing the cysts of the parasites with food or drink and not the active vegetative forms of *E histolytica* which are non infective and destroyed by the gastric juice Tanks rivers ponds wells and other sources of water supply polluted with infected cysts are the common sources of infection The sources of water supply may be polluted by a sewage being washed into them with rainfalls or by the washing of clothes and linens soiled with stools of patients suffering from amœbic dysentery or by fæces being directly thrown into water

3 FLIES Flies play an important role in the dissemination of the infection They carry the cysts from the stool to the food stuffs directly on their feet or by feeding on fæces containing cysts of *E histolytica* and then regurgitating the same on the food stuff or the cysts passing uninjured through their intestines may be deposited on food or drink with the fæces

4 CONTAMINATED VEGETABLES Fresh vegetables growing in infected soil may be contaminated and be a source of infection

5 DUST Dust probably plays no part in the dissemination of the disease because the cysts are rapidly killed by desiccation

PATHOLOGY

After being swallowed the infective mature tetra nucleate cyst passes through the stomach unaffected by the gastric juice In the small intestine the cyst wall dissolves under the action of the pancreatic juice and a tetra nucleate amœba is liberated (Fig 3) Each of its four

nuclei divides into two thus giving rise to 8 uni nucleate amœbulæ all of which become motile and by their pseudopodial movement pass on to the colon and lodge themselves in the mucous membrane Occasionally they enter the mucous membrane of the lower end of the ileum Some may

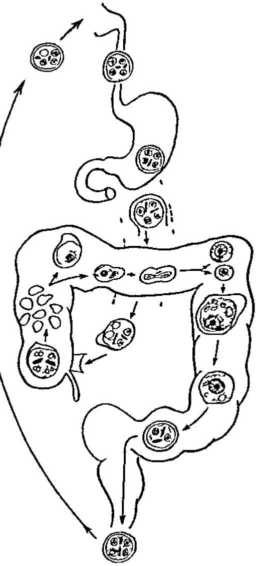


FIG. 3 Diagrammatic representation showing the fate of the infective cyst, after being swallowed.

escape into the lumen of the colon and pass out with the stools Others penetrate through the crypts of Lieberkuhn to the submucous layer of the colon and here they multiply by division secrete a powerful proteolytic enzyme dissolving the surrounding tissues and produce the ulcerations

ACUTE AMŒBIC DYSENTERY The earliest lesions consist of small superficial congested areas and/or ulcers involving only the mucous membrane Later the characteristic lesions which indicate the site of gelatinous necrosis in the submucous coat appear as small round yellowish elevations surrounded by a ring of congestion in the mucous membrane of the colon The centres of these elevated areas gradually slough off thus exposing the base of the ulcer which is in the submucous layer while the surrounding mucous membrane remains as an inflamed ring round the breach through which necrotic tissue projects into the lumen of the gut and the inflammatory exudations pour into the lumen of the colon The ulcers may be localised as solitary ulcers not larger than pins heads or they may be diffuse and extend over areas of varying sizes communicating with one another by sinuses burrowing under the mucous membrane A typical ulcer of amœbic dysentery consists of a small break in the mucous membrane and a base extending laterally in the submucous layer undermining the mucosa and thus giving rise to an ulcer with over hanging edges In vertical sections these ulcers are flask shaped The ulcers begin in the cæcum which is most commonly involved and they are scattered throughout the ascending colon rectum sigmoid and transverse colon Occasionally the appendix is also involved The intervening mucous membrane between the ulcers remains healthy Symptoms of amœbic dysentery are produced only when the ulcers are sufficient in number and when the local and general resistance of the host is lowered for any reason In severe cases the process of cytolysis and necrosis extends to the muscular coat and even to the peritoneal layer and may cause perforation with localised or generalised peritonitis A fatal peritonitis may also be due to acute sloughing and massive gangrene of the gut Rarely severe hæmorrhage may occur due to erosion of a small arteriole at the base of an ulcer

CHRONIC AMŒBIC DYSENTERY The ulcers are a few in number with raised thickened edges smaller in size and show varying stages of necrosis and healing There is a marked thickening of the submucous and mucous coats of the colon which may ultimately have almost a cartilaginous consistency Such a localised thickening may closely simulate carcinoma of the bowel Areas where the ulcers have healed

are oval and pigmented and depressed scars are often seen The formation of dense scar tissue leads to occasional contractures and sacculations of the gut There may also be adhesions between the proximal loops of the colon or between the peritoneal coat and the omentum the liver and the spleen

CARRIERS. The idea that an infection with *E histolytica* would cause only amoebic dysentery and liver abscess and nothing else is wrong The carrier condition though recognised was supposed to be an instance of almost perfect symbiosis between the host and the parasite without the production of any intestinal lesions We now know that even in absence of symptoms the carrier state is very commonly associated with ulcerative lesions of the colon and lesions in other organs and tissues

In such cases however the ulcers are usually a few superficial and localised to the cæcum or sigmoid In a large number of so called carriers there may be extensive lesions in the colon

AMŒBIC HEPATITIS AND LIVER ABSCESS *E histolytica* lying either at the base of amœbic ulcers specially of the cæcum and ascending colon or embedded in the submucosa without any obvious superficial ulceration of the mucosa invade the small tributaries of the portal vein in the sub mucous coat and are carried as emboli to the liver Apart from the embolic infection the liver may in some cases get involved through the peritoneal cavity On reaching the liver most of the *E histolytica* undergo degeneration or they are destroyed by tissue reactions Those which escape multiply and cause cytolysis of the hepatic tissue and give rise to small scattered greyish areas of necrosis (miliary abscesses) surrounded by a zone of hyperæmia Later on the necrotic areas described above liquefy at the centre gradually spread by further cytolysis and coalesce with neighbouring new necrotic foci by the destruction of the intervening septa and form a big ragged abscess cavity Around this there is a marked proliferation of the connective tissue cells forming a dense fibrous wall The contents of such a cavity are usually nonpurulent but chocolate coloured and mixed with small blood clots streaked with yellowish mucoid material due to presence of blood necrosed liver cells and cytolysed tissues *In case of secondary infection the contents are purulent and show a* large number of bacteria *e g* hæmolytic streptococci staphylococci or *Esch coli* The amœbæ which are absent in the contents of the abscess are present in the pus and the necrosed tissues from the walls of the cavity

Liver abscesses are often single. When single the abscess is usually situated in the right lobe of the liver near the dome of the diaphragm or on the under surface near the hepatic flexure. The liver shows varying degrees of enlargement associated with fatty change.

LUNG ABSCESS. There are two varieties of pulmonary amoebiasis primary and secondary. The primary variety is characterised by the development of small broncho-pneumonic areas due to the embolic invasion of the pulmonary circulation by *E. histolytica* from the bowel wall. Subsequent necrosis of these areas form small abscesses. The secondary is due to liver abscess which may invade the lungs and the pleura by contiguous spread or rupture and thus cause a lung abscess or an empyema.

AMOEBIASIS OF OTHER ORGANS. Amoebic abscess of the brain which is usually single is a rare complication. It is secondary to an abscess of the liver or the lung. Rarely abscesses of the spleen, kidney, suprarenal, seminal vesicles and testicles may occur. Amoebiasis cutis with punched out ulcers or gangrenous lesions of the skin may occur near a discharging liver abscess, sinus in the sacral region and in the abdominal wall near a colostomy wound.

CLINICAL MANIFESTATIONS

ACUTE AMOEBIC DYSENTERY (MILD OR MODERATE TYPE)

INCUBATION PERIOD. The period from the time of swallowing the cyst till the appearance of symptoms called the incubation period is very prolonged in amoebic dysentery. It varies from 1 week to 3 months.

MODE OF ONSET. Onset of the attack is usually gradual. It usually begins as a mild diarrhoea which turns in a few days into an acute dysentery characterised by the passage of blood and mucus in stool associated with abdominal pain, griping and rarely some degree of tenesmus and straining if the rectum is involved. In some cases the onset of the dysenteric symptom is sudden.

FEVER. Pyrexia is absent or slight in most cases unless there are some complications such as hepatitis and liver abscess. There is no sign of toxaemia in an uncomplicated case.

GASTROINTESTINAL SIGNS AND SYMPTOMS. The tongue may be slightly coated. *Often there is loss of appetite occasionally associated* with nausea and vomiting. On palpation tenderness may be elicited over the caecum, transverse and sigmoid colon which may be thickened

are oval and pigmented and depressed scars are often seen The formation of dense scar tissue leads to occasional contractures and sacculations of the gut There may also be adhesions between the proximal loops of the colon or between the peritoneal coat and the omentum the liver and the spleen

CARRIERS The idea that an infection with *E histolytica* would cause only amœbic dysentery and liver abscess and nothing else is wrong The carrier condition though recognised was supposed to be an instance of almost perfect symbiosis between the host and the parasite without the production of any intestinal lesions We now know that even in absence of symptoms the carrier state is very commonly associated with ulcerative lesions of the colon and lesions in other organs and tissues

In such cases however the ulcers are usually a few superficial and localised to the cæcum or sigmoid In a large number of so called carriers there may be extensive lesions in the colon

AMŒBIC HEPATITIS AND LIVER ABSCESS *E histolytica* lying either at the base of amœbic ulcers specially of the cæcum and ascending colon or embedded in the submucosa without any obvious superficial ulceration of the mucosa invade the small tributaries of the portal vein in the sub mucous coat and are carried as emboli to the liver Apart from the embolic infection the liver may in some cases get involved through the peritoneal cavity On reaching the liver most of the *E histolytica* undergo degeneration or they are destroyed by tissue reactions Those which escape multiply and cause cytolysis of the hepatic tissue and give rise to small scattered greyish areas of necrosis (miliary abscesses) surrounded by a zone of hyperæmia Later on the necrotic areas described above liquefy at the centre gradually spread by further cytolysis and coalesce with neighbouring new necrotic foci by the destruction of the intervening septa and form a big ragged abscess cavity Around this there is a marked proliferation of the connective tissue cells forming a dense fibrous wall The contents of such a cavity are usually nonpurulent but chocolate coloured and mixed with small blood clots streaked with yellowish mucoid material due to presence of blood necrosed liver cells and cytolysed tissues In case of secondary infection the contents are purulent and show a large number of bacteria *e g* hæmolytic streptococci staphylococci or *Esch coli* The amœbæ which are absent in the contents of the abscess are present in the pus and the necrosed tissues from the walls of the cavity

a pyrexia may give rise to difficulties in diagnosis A wrong diagnosis of tuberculo is is often made We believe that a certain percentage of the cases of obscure pyrexia in the tropics is contributed by chronic intestinal amœbiasis and that careful and repeated examinations of the stools would reveal the true nature of the pyrexia At the same time we would emphasize that the presence of a few vegetative or cystic forms of *E histolytica* in the stools should not too readily be accepted as the only explanation of an obscure pyrexia

Gastrointestinal Symptoms 1 *Irregularity of bowels* Some patients may complain of constipation for which he has often to take purgatives Some often may complain of constipation alternating with diarrhœa characterised by frequent loose stools containing mucus A few may get 2 to 3 stools every day with adherent mucus in them Others have to pass stools in about half to one hour after meals due to the increased gastrocolic reflex

2 *Abdominal pain* The patient often complains of a vague uncomfortable feeling or distinct colicky pain in the abdomen 1 to 4 hours after meals giving rise to the su picion of a gastric or duodenal ulcer and not infrequently he undergoes an operation without any relief of his symptoms The pain is due probably to the presence of lesions and subsequent adhesions in the hepatic and splenic flexures or may be due to a reflex pyloric spasm

The pain in the abdomen may be localised in the right iliac region paroxysmal in character appearing usually 4 to 5 hours after meals and simulating the clinical picture of chronic appendicitis Sometimes pain may be referred to the right shoulder and may lead to a wrong diagnosis of cholecystitis or cholelithiasis

3 *Digesti disturbance* (i) *Appetite* The appetite is capricious Sometimes the patient suffers from loss of appetite for days at other times he feels exceedingly hungry

(ii) *Nausea* It is usually complained of immediately before or after meals

(iii) *Flatulence* It often appears immediately or 4 to 6 hours after meals and may cause a sense of discomfort or sometimes a colicky pain which is relieved by evacuation or by passage of flatus

(iv) *Heart burn and acidity* These symptoms are usually present They are caused more by the presence of organic acids *e g* lactic or butyric acids in the stomach as a result of fermentation than by the presence of hyperchlorhydria

The liver may also be palpable and tender in some cases The stools are fairly large in amount and chocolate-coloured due to the presence of much dark and altered blood which causes an offensive smell The stools almost always contain fæcal matter and not infrequently blood streaked mucus scattered throughout the fæcal mass The reaction of the stools is acid Their number is usually 4 or 5 and very seldom exceeds 10-12 in 24 hours In very acute cases it may be more

LABORATORY FINDINGS *Blood* Examination of blood may show a moderate leucocytosis of 8000 to 15 000 per c mm with no proportionate increase of polymorphonuclear cells but with a very slight increase of eosinophils

ACUTE AMŒBIC DYSENTERY (FULMINANT OR GANGRENOUS TYPE)

MODE OF ONSET It is either a sudden primary attack or may be an acute exacerbation of a chronic dysentery

FEVER. Moderate pyrexia is present in association with marked prostration and toxæmia

ABDOMINAL SYMPTOMS AND SIGNS Abdominal pain and tenderness are marked Signs of peritonitis may be present The stools are very offensive and may be 20 or more in 24 hours They may contain little or no fæcal matter may be frankly hæmorrhagic and contain gangrenous sloughs

LABORATORY FINDING *Blood* Marked leucocytosis is usually present

CHRONIC AMŒBIASIS

Under this heading we include (1) chronic amœbiasis with dyspeptic symptoms (2) chronic amœbic diarrhœa (3) chronic amœbic dysentery and (4) chronic amœbic hepatitis

1 CHRONIC AMŒBIASIS WITH DYSPEPTIC SYMPTOMS *General Appearance* The patient is generally a lean thin and slightly anæmic individual with a muddy complexion Some individuals may however be well nourished and even obese

Fever Fever is not common unless there is an associated hepatic involvement or a secondary bacterial infection If present it is not usually perceived by the patient but i detected on carefully recording the temperature at 4 hourly intervals It is generally a low irregular type of fever with almost daily rises up to 99 100°F especially towards the evening and it may continue for a long time leading to marked weakness and prostration In the absence of any localising sign or symptom in bowels liver lungs or elsewhere such

III Chronic Amœbic Dysentery With prompt and efficient specific treatment an acute attack of amœbic dysentery may be completely cured in some but unfortunately majority show an apparent clinical cure and come back with acute dysenteric symptoms sooner or later Patients in whom the bowel symptoms persist for a month or more may be considered as chronic cases There are very few diseases that so frequently pass into a chronic stage as amœbic dysentery which may continue for months and years

We have seen medical practitioners as patients who have been suffering from recurrent attacks of dysentery for the last 20 25 years This chronic form of amœbic dysentery may result from the ordinary acute type passing into a chronic state or it may start from the very beginning as a mild infection associated with occasional diarrhœa but with no symptoms of acute dysentery The special clinical features of chronic amœbic dysentery are as follows

1 Recurrent attacks of dysentery with symptoms akin to an acute amœbic dysentery The quiescent intervals are characterised by constipation or diarrhœa

2 Emaciation and asthenia

3 Fever is slight or absent unless complicated with hepatic involvement

4 Presence of colicky abdominal pain associated with tender areas over the cæcum ascending transverse and sigmoid colon

5 Localised thickening of the cæcum sigmoid ascending and descending colon The thickening may involve the whole of the large intestine

6 Varying grades of anæmia of hypochromic microcytic type Occasionally macrocytic anæmia has been noted by us

7 Leucocyte count is usually normal The presence of even slight leucocytosis in presence of marked anæmia is a presumptive evidence of a liver abscess

IV Chronic Amœbic Hepatitis Repeated small embolic infections of the liver *via* the portal blood stream by *E histolytica* lying in the thrombosed veins at the base of the dysenteric ulcer produce frequently a diffuse and uniform congestion and swelling of the liver *i e* a hepatitis It is now believed (from positive hepatic function tests) that involvement of liver in amœbiasis is more common than any overt clinical sign would indicate

Acute Form It occurs in course of acute amœbic dysentery or diarrhœa or may follow a recent attack The clinical features consist

Abdominal Signs 1 The cæcum seems to be always full and is most easily palpable with a good deal of gurgling It is perhaps due to the checking of the normal peristaltic waves at the ulcerated sites and the damming back of the intestinal contents into the cæcum leading to a chronic cæcal stasis The cæcum may be so much thickened at times that the presence of associated wasting and occasional diarrhœa very often gives rise to the suspicion of a tuberculous cæcum or in an elderly person of a malignant disease of the cæcum

2 The sigmoid colon is markedly thickened and may be rolled under the fingers in many cases

3 Tenderness may be elicited (*a*) over the cæcum and asceding colon (*b*) over the appendicular region (*c*) around the umbilicus (*d*) over the sigmoid and (*e*) over the liver and gall bladder areas

Nervous Symptoms The patient frequently complains of a dull headache usually over the frontal region He seems to be most slack and irritable He often remains morose and melancholic and tries to avoid society He loses all interest in the world except in his abdominal condition He becomes bowel conscious and always worries about his intestines and thinks he has got abdominal cancer He worries about his heart and bloodpressure and suffers from palpitation vasomotor disturbances and extrasystoles There may be loss of sexual desire and he thinks he has developed impotency Thus by degrees the patient passes into a state of constant anxiety and morbid dread and then into a condition of confirmed tropical neurasthenia

Other Symptoms Muscular aches neuralgic pains sciatica lumbago and synovitis of single or multiple small joints may be present in some These symptoms may be allergic in nature as a result of recurrent secondary infections of the amœbic ulcers with streptococci some of which may escape into the blood stream through the breach in the mucous membrane of the colon and produce transient bacteriæmia

A few other conditions may not infrequently be associated with chronic amœbiasis *e g* asthma and leucoderma and they may show an improvement under treatment with amœbicidal drugs

II CHRONIC AMŒBIC DIARRHŒA There are recurrent attacks of diarrhœa alternating with constipation or normal bowel movements Each attack of diarrhœa may last for a few days to a few weeks The stools are usually 4-6 in number but may be more in 24 hours Abdominal pain with symptoms of flatulent dyspepsia are frequently present Other abdominal and nervous symptoms as have been described in carriers are more often seen in this group of cases

1 History of dysentery is obtainable in about 50 per cent of cases 6 months to 14 years prior to the appearance of symptoms of hepatic involvement

2 History of previous attacks of diarrhœa is as frequently obtained as a history of dysentery

3 Low intermittent or remittent pyrexia in about 66 per cent of cases Hectic fever in advanced cases Rigors and sweating during sleep are suggestive of suppuration

4 Emaciation associated with anæmia and slight jaundice—more frequently present in cases of abscess formation

5 Presence of stabbing pains over the liver region The shoulder pain is present in about 25 per cent of cases

6 Great enlargement of the liver with marked tenderness on palpation or heavy percussion The enlargement is frequently down wards less frequently upwards and downwards or only upwards

7 A localised tender swelling connected with the liver may be present in the epigastrium the right hypochondrium or in the lower intercostal spaces It indicates abscess formation Presence of loca lised œdema of the chest or abdominal wall over the enlarged liver is suggestive of liver abscess

8 Dry painful cough associated with congestion of the right lung base with or without pleurisy is often present Displacement of the heart to the opposite side or upwards may occur in cases of a large hepatic abscess

9 The usual leucocyte count is 15 000 30 000 per c mm A leucocytosis above 20 000 per c mm is very suggestive of liver abscess but not pathognomonic In the differential count the relative increase of neutrophils is never so high as in pneumonia empyema or other pyogenic infections We have seen a few cases of liver abscess with a leucocyte count of 5000-7000 per c mm in markedly anæmic cases

10 Presence of *E histolytica* cysts in stools in 45 per cent of cases

11 Elevation and fixation or restricted movement of the right dome of the diaphragm or of th left dome in cases of involvement of the left lobe of the liver as seen by fluoroscopy The elevated diaphragm with some obliteration of the cardiohepatic angle may be seen on a skiagram In very chronic cases a circular opaque shadow with partly calcified margins may occasionally be seen in the hepatic area

of (*a*) high and intermittent or irregular remittent fever associated with rigor during the rise and sweating during the fall of temperature (*b*) marked pain in the right hypochondrium with enlarged and tender liver (*c*) slight icterus of the conjunctivæ (*d*) referred pain over the right shoulder girdle or even the left in case of a left lobe abscess (*e*) deficient breath sounds over the right lung base (*f*) tenderness and thickening of the cæcum and ascending colon (*g*) marked leucocytosis 15 000-30 000 with a polymorphonuclear cell count of 80-90 per cent

In the fulminant types of acute amœbic hepatitis associated more often with the gangrenous type of amœbic dysentery the liver is riddled with numerous scattered foci of suppuration Death occurs in such cases within a fortnight from the onset of symptoms

Subacute Form It is characterised by (*a*) insidious onset (*b*) anorexia with or without nausea and progressive loss of weight (*c*) heaviness or pain in the right hypochondriac region or epigastrium or the pain may be referred to the right shoulder (*d*) fever usually of low remittent type (*e*) moderately enlarged and tender liver (*a*) moderate leucocytosis with a polymorphonuclear cell count of less than 70 per cent and (*g*) rarely jaundice

Chronic Form The usual clinical features are (*a*) history of a previous dysentery or recurrent attacks of diarrhœa (*b*) sense of tired ness (*c*) pallor and sallow complexion (*d*) constant dull ache over the liver (*e*) anorexia (*f*) liver just palpable and tender (*g*) tender and thickened cæcum and ascending colon (*h*) leucocyte count normal and (*i*) absence of fever and jaundice

AMŒBIC LIVER ABSCESS *Synonyms* Suppurative amœbic hepatitis Tropical liver abscess

Amœbic liver abscess occurs in cases where the embolic spread leads to a local accumulation of amœbæ causing thrombosis in a portal radicle and consequent necrosis of the surrounding tissues associated with cytolysis An abscess formation is the usual result In 70 per cent of cases the abscess is single Of these 84 per cent are in the right lobe of the liver

The highest incidence of abscess formation is between 21-40 years (70 per cent) about 5 per cent below 20 and 5 per cent above 50 years

Symptoms and signs are almost the same as those of amœbic hepatitis The following are the distinctive clinical features of abscess formation

PROGNOSIS

Before the introduction of emetine in the treatment of amœbic dysentery by Rogers in 1912 the prognosis of the disease was always very grave Complications like acute hepatitis and liver abscess were very common and often fatal At present the prognosis under treatment is however very good specially in the acute type of cases excepting the fulminating and gangrenous types which cause death from toxæmia and peritonitis Spontaneous recovery may occur in a fair number of cases In no other disease the medical treatment gives such immense relief to the patient with a rapid improvement of the clinical condition In many cases the infection runs a very chronic course for months or years characterised by periods of quiescence alternating with those of recurrent attacks of dysentery or diarrhœa and resulting in chronic invalidism The treatment of such chronic relapsing cases is very difficult and in most of them it fails to cause a complete and permanent cure

DIAGNOSIS

In the diagnosis of amœbiasis it is essential to remember that no group of clinical symptoms or signs is pathognomonic and that the demonstration of *E histolytica* in stools exudates or tissues of the patient is the only reliable method A correlation of the clinical data with the laboratory findings is very important in arriving at a correct diagnosis which may be based on the following criteria

ACUTE AMŒBIC DYSENTERY *Clinical Data* 1 Insidious onset

2 Fever—slight or none in absence of a complication such as hepatitis

3 Absence of toxæmia in most cases

4 Tenesmus—rare unless the rectum is involved

5 Physical signs—thickening and tenderness over the cæcum and ascending colon less frequently over the transverse and sigmoid colon

6 Liver may be palpable and tender

7 Stools—number—usually less than 15 odour—offensive colour—chocolate coloured due to presence of dark altered blood mixed with fæcal matter which is rather copious reaction—acid pH—6 5

Laboratory Data Microscopic examination of the stool shows

1 Presence of actively motile *E histolytica* with ingested red cells in a smear from a specimen of freshly passed stools

2 Characteristic cellular exudate (*a*) Scanty polymorphonuclear cells (only 7 5 per cent)

12 Absence of prompt response to a course of emetine therapy in a case of hepatitis is a strong evidence of liver abscess

COMPLICATIONS

COMMON 1 Hepatitis acute or chronic is the most common complication

2 Liver abscess occurs in 2 5 per cent of cases of amœbiasis observed during life It is present however in 15 19 per cent of autopsy cases of amœbic dysentery

3 Lung abscess frequently empyema and pneumothorax occasionally and pyo pericardium rarely secondary to rupture of liver abscess Rupture may also occur into the stomach duodenum hepatic flexure of colon peritoneal cavity and through the skin of the abdominal wall

4 Localised peritonitis

5 Appendicitis—in many cases the appendicular symptoms are not associated with an amœbic ulceration of the appendix

6 Supervention of bacillary dysentery

RARE 1 Amœbic granuloma or amœboma—In patients suffering from chronic intestinal amœbiasis a hard indurated tumour may be present in the cæcum transverse colon sigmoid or rectum The tumour is usually sausage shaped and varies in size from day to day It resembles a malignant growth in older people and tuberculoma in the young In absence of the causative organisms in the stools differentiation is difficult

2 General peritonitis

3 Intestinal hæmorrhage and perforation—usual sites of perforation in order of frequency are cæcum sigmoid rectum and appendix

4 Pericæcal or pericolic abscesses following perforation

5 Abscess of the brain—very rare

6 Abscess of the spleen and kidneys—very rare

7 Amœbiasis cutis

SEQUELÆ

1 Chronic recurrent diarrhœa—a very common sequel as a result of the replacement of the normal mucous membrane of the colon by scar tissue and subsequent interference with the absorption of fluids

2 Distension and sacculation of the gut leading to intestinal stasis

3 Cicatricial contracture and stenosis of the gut giving rise to a partial obstruction and hence chronic constipation

4 Anxiety neurosis

(*b*) Cysts of *E histolytica* which are typically tetra nucleate in the mature stage—very commonly found in the chronic cases

(*c*) Charcot Leyden crystals Most authorities however do not consider that their presence alone is diagnostic of an amœbic infection

A sample of freshly passed stool obtained after a saline purge should be examined for vegetative forms of *E histolytica* in chronic cases Detection of cysts of *E histolytica* in the stool is not very easy Typical portion of a good specimen of stools thin emulsion a good lens and patience are the four most important factors for their detection The examiner must not be satisfied with a single negative finding Mere detection of a cyst is not enough to show the infection with *E histolytica* The examiner must be certain that the cysts are those of *E histolytica*

Technique of Stool Examination Two preparations of stools should be examined in each case for the study of the amœba one specimen made with normal saline and the other with iodine solution (iodine 1 g potassium iodide 2 g water 100 c cm) The saline preparation shows the chromatoid bars inside the cysts and the vegetative forms whereas the iodine preparation shows clearly the glycogen and the nuclei in the cysts which are stained light brown and yellow respectively The sample of stool should be taken after a saline purgative and the portion of fæcal matter containing blood streaked mucus examined as fresh as possible because *E histolytica* dies very quickly and care should be taken that the stool is not mixed with urine or any antiseptic

Cultural Examination of Stool Positive results are obtained in a higher percentage of dysentery cases by this method than by microscopy It is however a difficult procedure requiring specialised knowledge and skill as well as the facilities of a well equipped laboratory

Every specimen of stool should be cultured for dysentery bacilli and streptococci even if the cysts of *E histolytica* be found as one should always remember that there may be mixed infection

Radiological Examination In chronic cases a series of radiographs taken at 12 18 24 and 36 hours after a barium meal show patchy filling defects in the cæcum or colon and loss of the normal haustration of the bowel The appearances are indicative of a chronic colitis but not diagnostic of an amœbic infection The radiological examination is therefore of limited value in the diagnosis of amœbiasis

(*b*) A large number of pyknotic bodies (nuclear remnants of cytolysed tissue cells and leucocytes)

(*c*) Macrophage cells absent or rare

(*d*) Red cells varying in size and shape and seen in clumps and rouleaux under the action of acid hæmatin formed from hæmoglobin due to the acid reaction of the stools of amœbic dysentery

(*e*) Numerous motile bacteria due to secondary infection

(*f*) Charcot Leyden crystals (chemically probably tyrosine) rarely *seen in the acute stage They begin to appear during convalescence and are the products of tissue digestion by E histolytica*

CHRONIC AMŒBIASIS *Clinical Data* 1 History of (*a*) Obstinate constipation (*b*) Alternate attacks of constipation and diarrhœa and (*c*) Previous dysentery in 40 per cent cases

2 Symptoms (*a*) Abdominal pain either half to one hour or four to six hours after meals not relieved by food (*b*) Flatulence *and (c) Heart burn and acidity*

3 Physical signs (*a*) Presence of anæmia with a sallow complexion (*b*) Localised thickening and tenderness over the cæcum and ascending colon frequently and over the transverse and sigmoid colon less commonly and (*c*) Enlargement and tenderness of the liver

4 Sigmoidoscopic Examination It offers valuable information in chronic amœbiasis where in about 75 per cent of cases characteristic small punched out ulcers with submucous hæmorrhages or scars of healed ulcers with a healthy mucous membrane intervening between them are seen in the rectum or lower part of the sigmoid An examination of the material from the scrapings of the ulcers may show *E histolytica* in cases where the stool examination has been negative In the carriers the ulcers are mostly situated in the cæcum and ascending colon and hence the value of a sigmoidoscopic examination in such cases is limited

Laboratory Data 1 Blood shows slight or moderate leucocytosis Marked leucocytosis with absence of a proportionate increase of polymorphs suggests liver abscess

Complement fixation reaction has been found to be of considerable diagnostic value in chronic amœbiasis *Cystic or vegetative E histolytica* were found in the stools of 89 7 per cent of the positive reactors

2 Stool examination Microscopic examination may show

(*a*) Vegetative forms of *E histolytica*—very seldom found in the carrier state

(*d*) Cholecystography may show a poor shadow or a non filling gallbladder filling defects or defective emptying after a fatty meal

CHRONIC AMŒBIC DYSENTERY OR DIARRHŒA This group has to be differentiated from the following

1 Helminthic dysentery

2 Tuberculous enteritis

3 Chronic bacillary dysentery

4 Sprue

5 Muco membranous colic—characterised by (*a*) High incidence in females (*b*) Presence of mucous casts (*c*) Presence of spastic constipation (*d*) Nervous constitution

6 Internal hæmorrhoids and inflamed piles

7 Rectal polyps

8 Malignant disease of the rectum

9 Syphilitic ulcer of the rectum

For the differentiation of the above diseases see the chapter on bacillary dysentery

CHRONIC AMŒBIC HEPATITIS This should be excluded from—

1 Malaria (see under malaria)

2 Kala azar (see under kala azar)

3 Pulmonary tuberculosis

(*a*) Characteristic physical signs in the lungs

(*b*) Presence of *M tuberculosis* in the sputum

(*c*) Parenchymal infiltrations in skiagram of the chest

4 *Esch coli* infection

PULMONARY AMŒBIASIS When an amœbic liver abscess ruptures into a bronchus there may be hæmoptysis which may lead to a wrong diagnosis of pulmonary tuberculosis

In other cases an amœbic lung abscess may be primary Pulmonary amœbiasis has to be differentiated from—

I PULMONARY TUBERCULOSIS

(*a*) *Primary pulmonary amœbiasis*—Though clinical and radiological pictures closely simulate pulmonary tuberculosis absence of *M tuberculosis* in the sputum and prompt response to emetine therapy are the differentiating features

DIFFERENTIAL DIAGNOSIS

ACUTE AMŒBIC DYSENTERY It has to be differentiated from the following

1 Acute bacillary dysentery
2 Malarial dysentery
3 Helminthic dysentery
4 Balantidial dysentery Characterised by presence of *Balantidium coli* in the stools Rare incidence
5 Intussusception

The differentiating features of the above diseases are described in a subsequent chapter on bacillary dysentery

CHRONIC AMŒBIASIS WITH DYSPEPTIC SYMPTOMS It simulates the clinical pictures of

1 GASTRIC AND DUODENAL ULCERS—characterised by

(*a*) Appearance of pain in the upper abdomen 1 to 3 hours after meals

(*b*) Relief of pain in duodenal ulcer by food and alkalis in gastric ulcer relief of pain by vomiting and alkalis

(*c*) Hæmatemesis and melæna

(*d*) Typical x ray findings with barium meal

(*e*) Prompt relief on strict dietetic therapy

2 CHRONIC APPENDICITIS

(*a*) Pain in the upper abdomen usually 4 to 5 hours after meals or may have no relation to meals

(*b*) History of previous attacks

(*c*) Localised tenderness in McBurney s spot

(*d*) Characteristic x ray findings (*i*) Appendix not mobile (*ii*) Tenderness over the appendix (*iii*) It does not fill properly and if it fills it does not empty even at the end of 48 hours (*iv*) The barium meal is held up in the distal part of the ileum even at the end of 6 hours

3 CHRONIC CHOLECYSTITIS AND CHOLELITHIASIS

(*a*) Upper abdominal pain in the epigastrium or right hypochondrium often immediately after meals or less frequently with no definite relation to meals Pain may be referred to the right shoulder History of biliary colic with or without jaundice may be present

(*b*) Symptoms of flatulent dyspepsia

(*c*) Gallbladder may be palpable and often tender

is one of the most frequent sequelæ which must be avoided for a month or so to prevent relapses Liquid paraffin in half or one ounce doses may be given every night to treat the constipation *Ishaphghula* seeds taken in doses of 2 to 4 heaped tablespoons suspended in a cup of water with the addition of a teaspoonful of sugar act as a laxative because of their mucilaginous content Abdominal massage along the course of the colon is also very useful in dealing with stasis

DIET In the acute stage all solid food should be withheld Light fluid diet *e g* citrated milk milk and barley milk and sago thin barley water lime whey may be freely given During convalescence bread egg fish chicken soft rice may be gradually added Excess of starchy foods such as potatoes bread and pastries fats indigestible or irritating food and alcohol should be avoided

In chronic amœbiasis the diet requires a careful consideration It should be adequate in calories and at the same time be rich in protein moderate in carbohydrate and poor in fat The protein requirements should preferably be met from mill skimmed milk fish and chicken or other lean meat Soft boiled rice and bread should be advocated for the supply of carbohydrates Green leafy vegetables should be sparingly used Fruits such as ripe bananas apples ripe *lals* or papaws are useful In case of constipation however bananas and apples are to be avoided In case of diarrhœa the pulp of baked *bel* sweetened with sugar should be taken in the morning

SPECIFIC TREATMENT

In 1902 Rogers showed that amœbic dysentery was very common in India and in 1912 he showed that the alkaloid emetine of ipecacuanha is a specific drug for the disease and for amœbic hepatitis At present there are too many drugs in the market which are all strongly advocated as the specific for the condition but it can be said without any fear of contradiction that no drug has yet been found which can replace emetine in the treatment of acute amœbic hepatitis and liver abscess

EMETINE It is an alkaloid of ipecacuanha and the salt preparation frequently used is the emetine hydrochloride which is soluble in water

Mode of action The mode of action of emetine in amœbic dysentery is not very clearly understood Vedder and Rogers think that emetine has a direct parasiticidal action on the amœbæ Dixon says that emetine is not very toxic to amœbæ According to him

	(b) Secondary pulmonary amœbiasis	Pulmonary tuberculosis
1	Clinical evidences of hepatic abscess—Present	Absent
2	Sputum — Chocolate coloured May contain *E histolytica*	No such colour *M tuberculosis* may be present
3	X ray—Show elevation and fixation of the right dome of the diaphragm with upward enlargement of the liver A dense shadow may be seen in the base of right lung The upper lung fields are clear	Parenchymal infiltration commonly in the upper zones cavity may be present
4	Emetine therapy — Prompt response	No response

II HYDATID CYST OF THE LUNG

(a) Presence of eosinophilia
(b) Presence of hooklets or fragments of cyst wall in the sputum
(c) Positive Casoni test
(d) Typical x ray picture—a cricket ball shadow

GENERAL MANAGEMENT

REST In cases of acute amœbic dysentery or diarrhœa patient is kept at bed rest till all symptoms disappear and course of emetine is over It takes about 10 12 days He must use the bed pan and urinal

WARMTH In the cold weather a flannel binder over the abdomen to avoid chill is very beneficial

CARE OF THE BOWELS A full dose of saline purgative *e g* an ounce of saturated solution of magnesium sulphate or an ounce of castor oil is given to flush out the colon as soon as the diagnosis is made On subsequent days 2 dr of sodium sulphate or magnesium sulphate in an ounce of water is given once every morning and bismuth carbonate in 1 2 dr doses is given three times daily for about a week This morning dose of saline purgative may not be necessary in some cases because emetine itself and other amœbicidal drugs have a tendency to produce diarrhœa

In chronic cases the action of the bowels tends to be irregular due to fibrosis of the ulcers and irregular peristalsis Constipation

5 Some may require prolonged and repeated administration of emetine which cannot be safely done for the cumulative effect of the drug

6 Presence of secondary infections of the amœbic ulcer with streptococci dysentery and coli group of organisms

Toxic effects Though emetine is the most valuable and useful drug in the treatment of acute amœbic dysentery it should not be administered in large doses or even in therapeutic doses for a long time as it has not only cumulative effects but also marked depressant effects on the heart and the nervous system Hence it is not permissible to administer more than one grain of emetine in 24 hours and nine grains in one course to an average adult Indian male

The toxic effects that are met with during emetine therapy may be described as below

1 *Gastrointestinal* (*a*) Anorexia (*b*) Nausea and vomiting (*c*) Abdominal pain (*d*) Diarrhœa which occasionally appears on the 5th or 6th day of treatment due to gastrointestinal irritation A mild diarrhœa is not a sign of intoxication rather it is considered to have a beneficial effect

2 *Cardiovascular* (*a*) Toxic myocarditis with weak heart sounds or fœtal rhythm and a weak small and rapid pulse (*b*) Irregularities of pulse *e g* extrasystoles and rarely auricular fibrillation (*c*) Fall of bloodpressure usually by 15 20 mm of mercury (*d*) Giddiness and feeling of faintness (*e*) Palpitation cardiac distress and dyspnœa (*f*) Occasional bradycardia due to heart block (*g*) Sudden cardiac failure from ventricular fibrillation

3 *Nervous* (*a*) Toxic polyneuritis causing dysphagia dyspnœa sense of constriction in the throat and chest paresis or paralysis of the muscles especially those of the arms and legs with tender calves ankle drop and wrist drop A scapulohumeral type of paralysis has been described We have seen the occurrence of a paralysis limited only to the serratus magnus on right side in a girl of 10 years on the fourth day of treatment with daily injections of 4 gr of emetine hydrochloride (*b*) Diminution of general muscular power associated with asthenia and tremors (*c*) Listlessness lethargy and somnolence

4 *Renal* Albuminuria rarely

5 *Cutaneous* (*a*) Oedema of the limbs or anasarca (*b*) Skin rashes (*c*) Petechial hæmorrhages (*d*) Abscess or cellulitis especially in debilitated individuals

emetine acts—(*a*) partly by a direct parasiticidal action and (*b*) partly by altered tissue reaction which is unfavourable to the growth of *E histolytica*

Dose

For adults of average weight	gr ½-1
For children of 9-12 years	gr ⅓
For children of 4-8 years	gr ⅙

Mode of administration Emetine is administered as soluble salt of emetine hydrochloride Emetine hydrochloride may be obtained in solution in ampoules or tablets of emetine hydrochloride Required dose may be dissolved in sterile water and injected by one of the following routes

(*a*) Intramuscular route This is the usual route but very painful

(*b*) Subcutaneous route It is less painful but local ecchymosis may occur

Duration of treatment In an adult the dose of gr 1 should be administered daily by the intramuscular route for six consecutive days In most cases of acute amœbic dysentery there is rapid clinical improvement in 3-4 days In some cases where the disappearance of symptoms is slow an interval of 3 days should be given after the sixth injection Again 3 further injections of gr 1 each are given in the following three days Thus one course should not exceed a total dose of 9 grains

In view of the cumulation of the drug in the tissues and its slow excretion a second course of emetine should not be given within three months of the completion of the first course

Causes of failure of emetine in the cure of amœbic dysentery

1 *E histolytica* lives in tissues and some in the lumen of the gut. One sixth of emetine is excreted with urine and five sixths into the bowels and during the process of excretion into the colon it acts on the amœbæ living in the tissues and not on those present in the lumen of the gut

2 In chronic cases the capillaries in the ulcerated areas are occluded due to fibrosis and so the drug cannot reach the parasites present in those ulcers

3 Emetine does not act effectively when the contents of the large intestine are very acid

4 Insufficient and improper use of emetine

Rectal route It is used in resistant cases only The drug is given as a retention enema at bed time in doses of 2 g in 200 c cm of warm 2 per cent sodium bicarbonate solution after a preliminary cleansing enema and this is repeated on alternate nights till five enemas have been retained

The retention of the enema is helped by the previous administration of gr 3 of sodium amytal to produce sleep

Advantages 1 Prompt clinical response 2 Fulfilment of the laboratory criteria of cure in 90 per cent of cases 3 Absence of toxic symptoms due to the wide margin of safety between the maximum therapeutic dose and the toxic dose 4 The administration by the oral route 5 Non interference with the patient s daily activities 6 Eradication of concurrent infections with other intestinal protozoa such as *Chilomastix mesnili Iodamœba butschlii Trichomonas Giardia intestinalis* etc

Contraindications 1 History of intolerance to arsenic 2 Presence of amœbic hepatitis and liver abscess 3 Presence of renal lesions 4 Presence of dermatitis

Toxic effects No toxic effects are usually observed except 1 Mild epigastric discomfort in some cases 2 Papular rash on skin —very rarely We have seen two cases of papular rash under carbarsone treatment and also a case of encephalopathy with recovery 3 Tubular nephritis and fatty degeneration of liver—recorded at autopsy of one case by Epstein

STOVARSOL (*Acetylaminohydroxyphenyl arsonic acid*) It contains about 27 per cent of arsenic and is available in the form of tablets of 0 25 g each

Dose

For adults 0 25 g twice a day for 10 days
For children of 2 5 years 0 125 g twice daily
For children of 1 2 years 0 05 g twice daily

Oral route The drug is given by the mouth in the dose of 1 tablet twice a day after meals for a period of 10 days It is better that the tablet is crushed before administration The course may be repeated after 3 weeks if necessary

Advantages 1 No necessity of confinement to bed 2 Carriers may be treated 3 Efficient amœbicide in 80 per cent cases after two courses

Indications of emetine therapy 1 Acute amoebic dysentery 2 Chronic amoebic dysentery with acute exacerbation 3 Hepatitis and liver abscess 4 Amoebic lung abscess 5 Amoebiasis cutis

Contraindications of emetine therapy 1 Amoebiasis of infants children below 4 years and very old individuals 2 Presence of marked asthenia and anaemia 3 Toxic myocarditis and presence of marked albuminuria If emetine has to be given it is advisable *to give in as small doses as possible* 4 *Ambulant patient* The patient should remain in bed during the period of emetine treatment Cases are on record that hearts have been permanently strained for want of this precaution 5 Appearance of cardiac symptoms and an increased pulse rate in course of emetine therapy

It should be emphasised that pregnancy is no contraindication to emetine therapy

Criteria of Cure Clinical Disappearance of all symptoms and signs that were present prior to treatment Normal sigmoidoscopic appearance

Laboratory Absence of *E histolytica* or its cysts in the stools on six consecutive examinations in course of three weeks after the cessation of treatment For all practical purposes this is the only reliable test of cure

According to this standard emetine cures one third of the cases improves the clinical condition in one third and exerts no beneficial effect in the remaining one third

CARBARSONE (*p carbaminophenyl arsonic acid*) It is a tasteless and odourless white crystalline powder containing 28 85 per cent arsenic almost insoluble in water but soluble in alkaline solutions *It is* available in capsules each containing 0 25 g of the powder and also in the form of tablet

Mode of action It has a specific action on the amoebae because of the high arsenic content

Dos

For adults 0 25 g or gr 3¾ twice daily
For children of 2 4 years 0 1 g
For children of 5 8 years 0 15 g

Mode of administration Oral route is the route of choice In adults a dose of 0 25 g is given as a tablet or in capsule after meals twice daily for a period of 10 15 days The course is repeated in resistant cases after an interval of ten days

Advantages 1 Prompt clinical cure 2 Fulfilment of the rigid laboratory test of cure in 81 per cent cases approximately 3 Extreme rarity of toxic symptoms

Toxic effects They are rare although the following have been reported to occur at times 1 Heaviness in the head 2 Palpitation 3 Dyspnœa 4 Excessive flatulence 5 Colic 6 Diarrhœa or Constipation 7 Presence of blood and mucus in the stools 8 Aggravation of pre existing bleeding piles

DIODOQUIN (*5 7 di iodo 8 hydroxy quinoline*) It differs from vioform in containing a second iodine atom in place of chlorine It contains 63 9 per cent of iodine

Mode of action It is said to be a better amœbicidal drug than vioform

Dose For adults 3 tablets (each tablet = 0 21 g) thrice daily for three weeks

Advantages 1 Prompt clinical cure 2 Tasteless 3 Not absorbed 4 Being nontoxic it can be given in a bigger dose for a longer period

Toxic effect The only toxic effects are pruritus ani and occasional headache

NIVEMBIN This is a combination of diodoquin and chloroquine sulphate Each tablet contains 0 3 g of diodoquin and 0 065 g of chloroquine sulphate (0 05 g base) The addition of chloroquine re inforces the efficacy of the drug by combating any systemic (epecially hepatic) invasion that may be present The dose is 2 tablets 3 times a day for 2-4 days reduced to 2 tablets twice a day altogether for about 2 weeks

CHINIOFON (B P) (*7 iodo 8 hydroxyquinolin 5 sulphonic acid*) It contains 28 per cent of iodine and is available in the form of powder tablets (gr 7½ each) and keratin coated pills (0 25 g each)

Dose For adults 2-4 pills thrice daily for 10 days

Mode of administration 1 *Oral route* In the beginning two pills three times daily are given to an adult The dose is gradually increased till 4 pills thrice daily are taken The treatment is continued for 10 days unless there is severe diarrhœa A second course is repeated if necessary at the end of a week In acute dysentery a preliminary course of emetine therapy should preferably precede the commencement of the treatment

2 *Rectal route* The drug is best given by this route as a retention enema of 6 ounces of 2½ per cent solution in warm water after a

Toxic effects Not infrequent commoner than carbarsone

1 Gastrointestinal tract—abdominal pain diarrhœa
2 Liver—jaundice occasionally
3 Kidneys—puffiness of the face albuminuria
4 Skin—erythematous rashes exfoliative dermatitis
5 Nervous system—polyneuritis rarely encephalopathy

We have seen the occurrence of exfoliative dermatitis polyneuritis and encephalopathy in course of treatment with this drug

MILIBIS This is a new compound of arsenic and bismuth containing 15 per cent arsenic and 41 88 per cent bismuth It is available under another proprietary name *iasept* each tablet containing 0 25 g of each of the drugs

Mode of action Specific action on *E histolytica*

Dose and administration 1 to 2 tablets three times a day orally after meals for 7 days The smaller dose is preferable

Advantages 1 Good response in subacute or chronic cases 2 Usual absence of toxic symptoms of the drug

Disadvantage Not suitable for acute cases

Another preparation containing 0 25 g of bismuth glycolylar sanilate and 0 075 g of chloroquine diphosphate in each tablet has been introduced under the trade name *neo iasept* Here also the dose is 1 2 (preferably one) tablets three times a day for 7 days Based on hepatic function tests the addition of chloroquine is for combating hepatic involvement which is believed to be a frequent occurrence even in the absence of clinical symptoms

VIOFORM (*Iodochlor hydroxyquinoline*) It is a greyish yellow powder containing about 40 per cent of iodine and almost insoluble in water Tablets are available containing sapamin for the emulsification and dispersion of the drug on the intestinal surface

Mode of action It is a very efficient amœbicidal drug owing to its high iodine content

Dose For adults 0 25 g four times daily

Mode of administration *Oral route* A tablet of 0 25 g is given orally four times a day after meals for a period of 10 days The stools assume a characteristic oily green appearance due to the drug After an interval of a week the drug is given in the same dosage four times daily for another period of 10 days After completion of this course cure results in about 81 per cent cases

Disadvantages 1 Necessity of rest in bed for at least two weeks during the treatment 2 Occurrence of toxic signs and symptoms *e g* marked nausea and diarrhœa loss of weight and a fall of bloodpressure 3 Refusal of the patients to follow the treatment

EMETINE PERIODIDE It is less toxic than E B I but equally effective In adults the dose is gr 3 daily in capsules for 10 days orally

KURCHI ALKALOIDS The active principles of kurchi bark are the alkaloids conessine and holarrhenine obtained from *Holarrhena antidysenterica* a small plant growing throughout India

Mode of action Conessine has been reported to have a specific action on *E histolytica* and it has been recommended in place of emetine Its action is however not so prompt as that of emetine and it takes slightly longer time to control the symptoms

Dose Conessine hydrochloride gr 1 daily

Mode of administration It is given by the intramuscular route daily in gr 1 doses for 10 days

Intravenous route is not to be adopted for depressant action on the heart

OTHER KURCHI PREPARATIONS (containing total alkaloids) A standardised liquid extract of kurchi can be given with beneficial results in 2 to 3 dr doses three times daily per mouth for 2 3 months in resistant cases Tabloids extract kurchi corticis of gr 5 each may also be given in doses of 2 to 3 tabloids three times daily

Advantages 1 It is cheaper than emetine 2 It can be given per mouth unlike ipecacuanha without any unpleasant symptoms

KURCHI BISMUTH IODIDE It is a combination of the total alkaloids of kurchi bark with bismuth carbonate and potassium iodide

The drug has been given by Acton and Chopra in doses of gr 10 twice daily for 10 days preceded by an alkaline mixture Good results have been reported in cases of both acute and chronic amœbic dysentery without producing gastro intestinal irritation or cardiac depression

It is available in the form of tablet of gr 1½ each (*kurchibide*) 2 tablets are given at a time 3 times daily for 10 days

BROAD SPECTRUM ANTIBIOTICS Both oxytetracyclin and aureomycin have been found to be effective in intestinal amœbiasis The usual dose is 0 25 or 0 5 g 6 hourly for 10 days The antibiotics have the special advantage that in addition to the amœbicidal action they also combat secondary bacterial infection Excessive cost is a disadvantage Besides relapse may occur unless other antiamœbic drugs are also used

preliminary cleansing enema of one pint of 2 per cent sodium bicarbonate solution an hour before The enema is continued for 10 14 days

Combined oral and rectal treatment is recommended specially in chronic amœbic dysentery

Advantages 1 Efficient amœbicide 2 Absence of any toxic symptoms 3 Suitable for treatment of carriers (Craig) and cases of amœbic diarrhœa and even acute amœbic dysentery

Disadvantages 1 Necessity of bed rest 2 High cost of the drug 3 *Occasional diarrhœa—lasting for 3-4 days*

RESOTREN This is a salt of 7 iodo 8 hydroxyquinoline-5 sulphonic acid (*yatren*) and chloroquine (*resochin*) base Each tablet contains 0 5 g of this salt The chemical combination is expected to control intestinal amœbiasis and any hepatic involvement simultaneously The drug has produced good result in acute and chronic intestinal amœbiasis but may cause or increase the existing diarrhœa

Dose 1 tablet after meals thrice daily for one week and twice daily for another week

Toxicity Diarrhœa griping pain

EMETINE BISMUTH IODIDE (E B I) It is a brickred powder containing approximately 30 per cent emetine It is available in the market in the form of powder and hard keratin coated pills

Dose 2 3 gr in adults

Mode of administration 1 *Oral route* Inspite of its nauseating taste *it should be given in the powder form as the pills are likely to* pass out with the stool undissolved in the bowel The powder is given 4 hours after the last meal on the first night in gr 1 dose and on subsequent nights in gr 2 doses (for average Indian) in cachet or gelatin capsules or suspended in one or two teaspoonfuls of liquid paraffin for 12 consecutive nights It frequently causes sickness To avoid it the patient should be given 10 or 15 minims of tincture of opium or gr 2 of phenobarbitone half an hour before retiring to bed and the drug should be administered as soon as *the patient is found drowsy so that* he will go to sleep without having any sickness During the course of this treatment there may be a mild attack of diarrhœa for which the treatment should not be suspended but it must be continued to be effective If *E histolytica* is still present in the stools after one course of treatment a second course may be repeated after an interval of three weeks

Advantages 1 Marked efficacy in cases resistant to emetine 2 Probable cure rate is 70-80 per cent

To summarise the following general routine may be followed in treating cases of amœbiasis

A *Acute amœbic dysentery* Emetine gr 1 intramuscularly daily for 6 days another three injections after 3 days rest (total 9 grains) This is followed by a course of vioform (40 tablets in 10 days) and then carbarsone (20 tablets in 10 days)

In children and asthenic cases it is better to avoid emetine They may be treated with an initial course of diiodohydroxyquinoline (D) and chloroquine (C) (1 8 g of D and 0 5 g of C daily for 2 4 days and then reduced to 1 2 g of D and 0 2 g of C altogether for 2 weeks) and followed by a course of carbarsone

B *Chronic amœbiasis without hepatitis* A course of vioform if necessary with chiniofon retention enema (specially in case of the ulceration seen by sigmoidoscopy) and followed by a course of carbarsone

Chronic amœbiasis with hepatitis A course of 9 injections of gr 1 each of emetine in the course 12 days as indicated above if necessary with chiniofon retention enema and followed by a course of vioform In children and asthenic patients emetine should be replaced by a course of chloroquine

SYMPTOMATIC TREATMENT

1 ABDOMINAL PAIN (*a*) Application of hot fomentation over the abdomen (*b*) Sedatives and antispasmodic mixtures containing bromide and tincture belladonna (*c*) Injections of atropine sulphate gr 1/100 hypodermically

2 TENESMUS (*a*) Starch and opium enema (*b*) Cocaine and morphine suppositories (*c*) Hypodermic injection of morphine hydro chloride gr ⅙ only in severe cases

3 DIARRHŒA Bismuth carbonate in 1 2 dr doses suspended in a cup of water is given three times a day to prevent the onset of diarrhœa or to control it by its soothing astringent action on the ulcers Even in absence of diarrhœa Deeks advocates the routine administra tion of large doses of bismuth subnitrate (bismuth carbonate is how ever preferred by most authorities) during the course of emetine therapy to enhance the action of emetine

Kaolin or colloidal kaolin in doses of 1 2 dr suspended in a cup of water may be given on an empty stomach as a substitute for bismuth carbonate with a view to adsorb the bacterial toxins

along with the antibiotics Heavy dose of vitamin B complex is required during this therapy

CHLOROQUINE This potent antimalarial has also been found to be very effective for metastatic amœbiasis It is rapidly absorbed and has little effect on intestinal amœbiasis It accumulates in the tissues and reaches high concentration in the liver Cases of amœbic hepatitis and liver abscess have been satisfactorily treated with a dose of 0 3 g (base) twice daily for two days followed by 0 3 g (base) once daily for two weeks

CHOICE OF DRUGS It is essential to remember that no single drug is efficient in eradicating the amœbic infection A suitable combination of two or more of the above mentioned specific drugs may be necessary

Acute Amœbic Dysentery 1 A cour e of emetine hydrochloride —6 9 injections of gr 1 each

2 A course of carbarsone or vioform—for 10 15 days after the cessation of emetine therapy

Chronic Amœbic Dysentery Stage of acute exacerbation Preliminary course of emetine followed by carbarsone or vioform or diodoquin

Quiescent stage Various combinations of drugs have to be used The one most often recommended but difficult to follow except in a hospital is emetine bismuth iodide orally with chiniofon retention enema This may be followed by vioform carbarsone diodoquin nivembin milibis or resotren orally

Treatment of chronic cases is still a difficult problem Secondary infections frequently complicate amœbic colitis and these patients often show mucus and pus cells persistently in their stools These cases show good improvement with a preliminary course of penicillin and sulphaguanidine The usual dose of fortified procain *penicillin 400 000 units daily together with sulphaguanidine in the dose* of 4 tablets (0 5 g each) 6 hourly is given for a period of five to seven days Oral streptomycin or a combination of streptomycin and sulpha guanidine may be used for the same purpose Administration of the broad spectrum antibiotics aureomycin and terramycin has the advantage that they combat the secondary infections and at the same time are active against amœbæ A conventional course of amœbicidal drugs may be given following their use Eradication of secondary infections definitely increases the cure rate by the routine amœbicidal drugs

(*iii*) In case of rupture of the hepatic abscess into the pleural cavity and into the neighbouring viscera

(*d*) Subsequent administration of amœbicidal drugs such as carbarsone or vioform to cure the associated intestinal amœbiasis

3 PULMONARY AMŒBIASIS A full course of emetine therapy is given as in amœbic hepatitis

4 CHRONIC AMŒBIC APPENDICITIS Preliminary emetine therapy is essential It is effective in most cases Surgical measures are to be adopted as a last resort

5 PERICOLIC ABSCESS The treatment is the same as above

PREVENTIVE MEASURES

It is a very difficult problem from economical considerations In view of our knowledge that infection occurs through contamination of food and drink with cysts of *E histolytica* preventive measures should consist of the following

1 Efficient disposal of sewage 2 Use of sanitary privies in rural areas 3 Protection of water supplies against fæcal contamination 4 Use of boiled drinking water in rural areas 3 Protection of all food and drink from flies 6 Avoidance of use of raw vegetables and fruits 7 Detection isolation and treatment of carriers This last measure is impracticable because of the heavy cost it entails on a community It should however be carried out wherever possible Carriers who serve as cool s or distributors of food or employees in a dairy should undergo treatment for eradication of the infection If it is not possible they should cleanse their hands scrupulously before preparing and serving food 8 Rigid observance of the elementary rules of personal hygiene and cleanliness 9 Dissemination amongst the public of the knowledge regarding the modes of infection in amœbiasis

J C B

TREATMENT OF COMPLICATIONS

1 Amœbic Hepatitis (*a*) A course of 9 injections of emetine hydrochloride in doses of gr ½ 1 according to the general state of the patient and his cardiovascular condition Chloroquine 0 3 g (base) twice daily for two days followed by 0 3 g (base) daily for 14 days is also effective and may be used instead specially if the general condition is weak The two may also be used together In some of these cases administration of chloroquine is followed by sweating and fall of bloodpressure

(*b*) Hot applications over the hepatic area

(*c*) Administration of a dose of saline purgative every morning to reduce portal congestion

(*d*) Subsequent eradication of associated intestinal amœbiasis by use of carbarsone or vioform

2 Liver Abscess (*a*) A preliminary course of emetine as indicated above should always be given in absence of urgent symptoms It has the following advantages

(i) It helps to differentiate a hepatitis from a liver abscess

(ii) It reduces the congestion of the liver and renders the subsequent *aspirations safer by lessening the risk of hæmorrhage*

(iii) It causes a liquefaction of the pus and renders the aspiration much easy

Liver abscess has also been successfully treated with chloroquine with or without aspiration

(*b*) Aspiration is done with a Potain s apparatus over the most tender point or in the 8th or 9th intercostal space under local anæsthesia in the anterior axillary line by means of a wide bored needle It may have to be repeated once or twice The presence of an up and down movement of the outer end of the needle indicates that it has entered the liver

(*c*) Open operation is rarely necessary the mortality rate being 50 60 per cent if due to secondary infection It is indicated under the following conditions

(i) When the aspirated liver pus shows presence of numerous pus cells and bacteriæ *e g* streptococci staphylococci or *Esch coli* Emetine with an antibiotic like penicillin or aureomycin depending on the type of organism may be tried in these cases

(ii) When the abscess is in the left lobe and not shut off by adhesions from the general peritoneal cavity

flagellates swim quite rapidly and are very active in fresh samples of stools

PATHOLOGY

The infection occurs due to ingestion of cysts only The intestinal mucosa is never invaded The glands of the small intestine however may remain packed with giardia Only superficial irritation leading to catarrhal enteritis usually occurs

The condition may be and usually is asymptomatic Massive infection gives rise to periodic attacks of diarrhœa with passage of mucus In children the stools are frothy resembling the stools of sprue syndrome

DIAGNOSIS

LABORATORY FINDING Demonstration of active motile flagellates or cysts in the stools

SPECIFIC TREATMENT

In adults oral administration of mepacrine hydrochloride 0 1 g three times a day for 5 7 days after meals is effective Relapses are common Treatment is often required to be repeated after 15 21 days

Camoquin tablet 0 2 g orally once a day after meals for 8 days has proved useful

L K G

CHAPTER II

GIARDIASIS

There are three common flagellates which inhabit the intestines of man. They are *Giardia intestinalis*, *Trichomonas hominis* and *Chilomastix mesnili*. The normal habitat of *Giardia intestinalis* is the upper part of the small intestine and the other two are found in the cæcum and colon. Of these *Giardia intestinalis* only is pathogenic to man.

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION. Giardiasis is common in England, Canada, and throughout the tropics.

AGE AND SEX INCIDENCE. Children are prone to suffer from giardiasis more than the adults. There is no sex or special race predilection.

CAUSATIVE ORGANISM. The organisms are intestinal protozoal parasites of man. They are pear shaped flagellates. At the anterior end

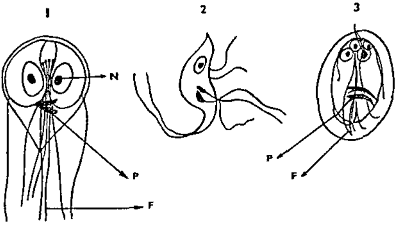


FIG. 4. *Giardia intestinalis*, free and encysted forms.
1. Active form. 2. Active form (side view). 3. Cyst with four nuclei. N.—Nucleus. P.—Parabasal bodies. F.—Flagella.

there are two oval nuclei within the sucking discs. There are characteristically curved parabasal bodies in the sytoplasm (Fig. 4). The

In 1897 98 Ross proved that the disease was transmitted by certain definite species of mosquito (now known as *Anopheles*) and conveyed to human host by the bite of infected mosquitoes

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION Malaria is the most common disease in the tropics and causes millions of death every year either directly or indirectly Malignant or subtertian malaria is specially confined to the tropics Benign tertian is relatively more frequent in the subtropics and in temperate countries where it is usually the commonest form but it also occurs in the tropics Quartan malaria which is the least frequent type and constitutes 20 25 per cent of malaria has a patchy distribution throughout the malarious areas of the world

In India—Nepal Bhutan Kashmir and areas over 6000 ft above sea level are non malarious Infection seldom occurs in India at a height over 6000 feet above sea level because of the low temperature at higher elevations In West Bengal Bihar and the Uttar Pradesh malaria is present in a moderate degree The Madhya Pradesh and Assam are intensely malarious In the East Punjab there is very slight malaria but at times there break out fulminating epidemics of malaria Certain places of West Bengal are intensely malarious

In Ceylon a severe epidemic of malaria with a high mortality broke out in 1934

In cold countries malaria is very rare

In Europe malaria occurs frequently in a mild form as in Holland Its incidence is at present much reduced in Spain Portugal and Italy which were heavily infected a few decades ago In New York malig nant tertian malaria is endemic In Central and East Africa the occurrence of malignant and benign tertian malaria is quite common

SEASONAL PREVALENCE Malaria is most prevalent in later months of rainy season and during the months which intervene between the rains and the winter because a higher atmospheric temperature is nece sary for the development of this parasite in the mo quito Infec tion begins in June or July and reaches its highest peak in October or even in early part of November Benign tertian infections eem to begin earlier in the year than malignant tertian

ATMOSPHERIC TEMPERATURE Temperature below 60°F and humidity below 63 per cent are unfavourable conditions for the infection as the malaria parasites do not develop in the mosquito under such adverse environment

CHAPTER III

MALARIA AND BLACKWATER FEVER

MALARIA

DEFINITION

Malaria is a specific fever caused by certain protozoal parasites of the class *Sporozoa* the suborder *Hæmosporidiida* and the family *Plasmodiidæ* whose definitive host is mosquito and intermediate host is man These parasites infect the red blood corpuscles produce anæmia enlargement of spleen and liver and give rise to periodic fever which is usually intermittent but may be remittent or continued It is nearly always febrile but it may be afebrile for a considerable period

The word malaria is derived from two Italian words—*malo* (bad) and *aria* (air) [This term was applied as the old belief was that the disease was due to the inhalation of poisonous emanations from marshy ground]

HISTORY

The disease was known even as early as the 5th century B C to Hippocrates who recognised some periodic fevers such as quotidian tertian and quartan but it is certain that these periodic fevers were not named malaria at that time

The name malaria was given to the disease by an Italian writer in 1753 but long before this a satisfactory method of treatment of the disease was found out In 1638 Countess Chinchon wife of a Spanish Viceroy of Peru suffering from intermittent fever was supposed to have been cured with the bark of an indigenous tree of Peru which was subsequently named cinchona in honour of the Countess

In 1820 quinine was isolated from the cinchona bark

In 1847 Meckel discovered the presence of characteristic pigment in the viscera *e g* spleen of persons who had died of malaria

In 1880 Laveran discovered the sexual forms of the malignant tertian malaria parasites in the human blood

In 1885 86 Golgi differentiated the quartan and the benign tertian parasites on their morphological character

In 1894 Manson suggested that mosquitoes might be the vectors of malaria but he thought that mosquito transmits the disease to people through drinking water containing infected mosquitoes

to grow at the expense of the hæmoglobin and develop into amœboid forms known as *trophozoites* In course of their growth the trophozoites

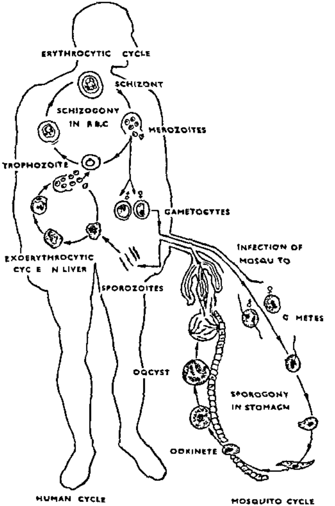


FIG 5 Sl ow g hagrammat cally the a exual cycle of development in human ho t and the sexual cycle in the mosquito

are pigmented and the red cells show certain changes such as enlargement or contraction pallor and regular or irregular stipplings which

RAINFALL High rainfall means a high malarial incidence but it is not true in all places In certain places such as Ceylon heavy rainfall flushes out the breeding pools of the mosquitoes and causes definite diminution in the malarial incidence

SOIL CONDITIONS A high subsoil water level means increased occurrence of malaria Presence of pits pools buildings bridges canals embankments and railways interfering with the natural surface drainage causes an increase of malaria Well drained uplands are generally free from malaria

ECONOMIC CONDITIONS Financial capacity of the people to live in better houses to use mosquito-nets to take quinine or to wear protective clothing is an important factor Increase of malaria makes the economic condition very poor and so the reverse is also true

RACE No race is immune to infection As a result of repeated infections in childhood the adult persons in an endemic or hyper endemic area are partly immune whereas the foreigners from non malarious areas are very susceptible

AGE AND SEX INCIDENCE In endemic and highly malarious areas young children are seen to be more common victims than the adults Both sexes are equally liable

CAUSATIVE ORGANISM There are four different species of malaria parasites

1 Benign tertian (*Plasmodium vivax*) 2 Quartan (*Plasmodium malariæ*) 3 Malignant tertian (*Plasmodium falciparum*) 4 Ovale tertian (*Plasmodium ovale*)

Man is also susceptible to experimental infection with *Plasmodium knowlesi* a parasite of monkeys

LIFE CYCLE *Asexual Cycle or Human Cycle* The malaria parasites undergo a pre erythrocytic cycle of development before entering the red blood cells The sporozoites introduced through the bite of an infected Anopheline are carried by the circulation to the liver cells where they develop through the pre erythrocytic cycle into a large number of merozoites (*cryptomerozoites*) which find their way to the circulation and invade the red cells (Fig 5) The pre erythrocytic stages of *P vivax* and *P falciparum* have been demonstrated in the human liver

The merozoites attaching to red blood cells develop into rings trophozoites and schizont (*Erythrocytic Cycle*) These rings which consist of a vacuolated cytoplasm and one or more chromatin dots begin

to gro at the expen e of the hæmoglobin and d velop into amœboid forms known as *tro, ho oites* In course of their growth the trophozoites

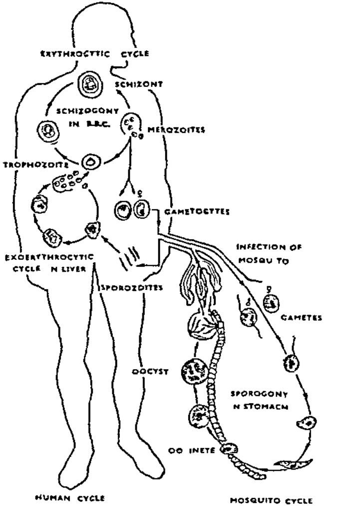


FIG. 5 Showing diagrammatically the asexual cycle or development in human host and the sexual cycle in the mosquito

are pigmented and the red cell show certain change such as enlarge ment or contraction pallor and regular or irregular tipplings which

RAINFALL High rainfall means a high malarial incidence but it is not true in all places In certain places such as Ceylon heavy rainfall flushes out the breeding pools of the mosquitoes and causes definite diminution in the malarial incidence

SOIL CONDITIONS A high subsoil water level means increased occurrence of malaria Presence of pits pools buildings bridges canals embankments and railways interfering with the natural surface drainage causes an increase of malaria Well drained uplands are generally free from malaria

ECONOMIC CONDITIONS Financial capacity of the people to live in better houses to use mosquito nets to take quinine or to wear protective clothing is an important factor Increase of malaria makes the economic condition very poor and so the reverse is also true

RACE No race is immune to infection As a result of repeated infections in childhood the adult persons in an endemic or hyper endemic area are partly immune whereas the foreigners from non malarious areas are very susceptible

AGE AND SEX INCIDENCE In endemic and highly malarious areas young children are seen to be more common victims than the adults Both sexes are equally liable

CAUSATIVE ORGANISM There are four different species of malaria parasites

1 Benign tertian (*Plasmodium vivax*) 2 Quartan (*Plasmodium malariæ*) 3 Malignant tertian (*Plasmodium falciparum*) 4 Ovale tertian (*Plasmodium ovale*)

Man is also susceptible to experimental infection with *Plasmodium knowlesi* a parasite of monkeys

LIFE CYCLE *Asexual Cycle or Human Cycle* The malaria parasites undergo a pre erythrocytic cycle of development before entering the red blood cells The sporozoites introduced through the bite of an infected Anopheline are carried by the circulation to the liver cells where they develop through the pre erythrocytic cycle into a large number of merozoites (*cryptomerozoites*) which find their way to the circulation and invade the red cells (Fig 5) The pre erythrocytic stages of *P vivax* and *P falciparum* have been demonstrated in the human liver

The merozoites attaching to red blood cells develop into rings trophozoites and schizonts (*Erythrocytic Cycle*) These rings which consist of a vacuolated cytoplasm and one or more chromatin dots begin

gives rise to sickle shaped sporozoites by nuclear division Later this mature oocyst ruptures with liberation of sporozoites which find their way through the body cavity into the salivary glands of the mosquito and lodge there The whole process takes about 10 to 12 days when the mosquito is capable of infecting a susceptible person The infectivity of the mosquito may last as long as 3 months

MODE OF INFECTION

Malaria is transmitted to human beings by the bites of certain species of female Anopheles which in their turn have been infected by feeding on persons who are carriers of gametocytes Transmission of malaria from the mother to the child by the placental route is rare in spite of numerous records of such instances in medical literature Congenital malaria may however occur in cases of failure of the barrier action of the placenta due to accidental tears or heavy infection of the placenta in 36 per cent of pregnant women infected with *P falciparum*

Blood transfusion provides another means by which transmission of malaria may occur Transfusion of serum or plasma is however safe

Transmission of malaria in drug addicts from the use of a com mon unsterilised syringe may occur

Artificial induction of malaria by injecting infected blood still remains a successful therapeutic measure in the treatment of neurosyphilis

For the continued existence of malaria in a locality the chain between man malaria parasites and mosquito must remain unbroken and if one of the links in the chain be missing malaria cannot exist thus there must be (1) susceptible human beings in the locality (2) gametocytes in the peripheral blood of infected person and lastly (3) suitable Anopheles mosquitoes in that area

It must be further emphasised that (1) all kinds of Anopheles mosquitoes cannot carry the disease (2) it is only the females of certain species of Anopheles which are responsible (3) the commonest carrier in India is *Anopheles culicifacies* *Anopheles stephensi* is also found as a carrier in some parts of India (4) these mosquitoes must have opportunities to bite carriers of gametocytes after which they must live for 15 20 days for the completion of the sexual cycle of the parasites and then bite some susceptible human beings

are helpful in the identification of the various malaria parasites (See Plate and Table I) Sooner or later nuclear division takes place and the trophozoite on maturity becomes a *schizont* (*schizogony*) The latter consists of a varying number (8 24) of nucleated segments called merozoites arranged round a residual mass of cytoplasm and pigment and enveloped by the red cell On gaining maturity the schizont ruptures and liberates into the blood stream every 48 72 hours according to the species of the parasite a swarm of little merozoites a large number of which is engulfed by the polymorphonuclear cells and monocytes (large mononuclear cells)

Some of them, however enter fresh red blood corpuscles and repeat the same developmental cycle until by the 14th day the concentration of parasites in blood is adequate enough (one thousand million parasites in *P vivax* infection according to Ross and Thomson) to reach the pyrogenic threshold and give rise to the first febrile paroxysm At some stage of the infection and usually after 8th 10th day of the first febrile attack the resistance of the host gradually increases and the conditions for the development of the parasites become unfavourable probably due to the administration of anti malarial drugs During this period the parasites *i e* some of the merozoites commence their sexual or *sporogony* cycle and *gametocytes* begin to appear in the peripheral blood

The new knowledge about the life cycle of malaria parasites has thrown some light on the causation of relapses It appears that in vivax malaria some of the cryptomerozoites enter fresh liver cells so that a persisting exo erythrocytic cycle continues and may periodically invade the blood stream In *P falciparum* malaria development in liver does not proceed further after the pre erythrocytic stage

Sexual Cycle The gametocytes (both male and female) which remain in the peripheral blood as inert foreign bodies and produce no symptoms are sucked in with blood by female Anopheles during their bite on the human carriers On reaching the stomach of the mosquito the female gametocyte undergoes maturation by changing into a spherical shape and extruding two polar bodies and forms the female gamete (*macrogamete*) The male gametocyte gives rise to 4-8 *microgametes* by the process of exflagellation The macrogamete is then fertilised by a microgamete and forms a *zygote* which soon changes into a motile body called *ookinete* (*sporogony*)

The latter bores its way through the stomach wall to rest under its outer layer and forms a small *oocyst* which gradually enlarges and

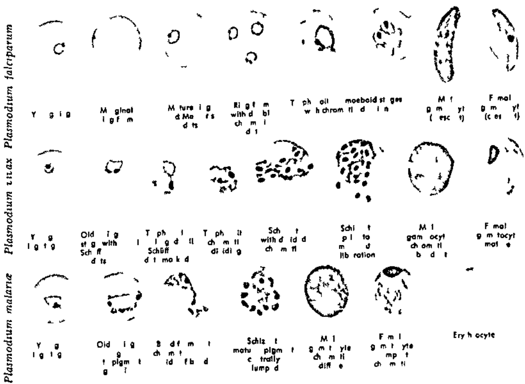

Plasmodium falciparum
Plasmodium vivax
Plasmodium malariae

TABLE I

DIFFERENCES IN CHARACTER OF THE FOUR SPECIES OF MALARIA PARASITES

	Benign Tertian	*Malignant Tertian*	*Quartan*	*Oval Tertian*
Trophozoite.	Blue signet rings relatively large round or oval Round chromatin dot in thin part of the ring Growing forms actively amœboid and irregular in shape with vacuoles and scanty cytoplasm	Blue ring smallest of all thin and hairlike with very scanty cytoplasm and often with two red chromatin dot Marginally attached rings (accoliform) and more than one ring in a red cell very common	Blue signet rings smaller but denser than [illegible] rings deep blue cytoplasm with large deep red chromatin Growing forms slightly amœboid band like or comet like	Ring like those of quartan parasites
Hæmozoin pigment.	Fine yellowish brown grains scanty but evenly distributed	Granular Brown	Coarse brown black granules in abundance	Blackish brown
Changes in infected red cells	Pale enlarged and stippled with Schuffner s dots	Usually unchanged shrinking crenation and polychromatophilia may be present Cleft like dots called Maurer s dots may be seen	Not enlarged Schuffner s dots usually absent Some observers have however described occasional stippling of red cell	Irregular and oval
Mature schizont	Large almost fills the enlarged pale red cell	Smaller than a red cell	Smaller than a red cell	Smaller than a red cell
Merozoite	14 24 (usually 18 20) arranged in an irregular grape like cluster	6 24 (usually 8 10) arranged in a grape like cluster Rarely seen in peripheral blood except in very severe cases	6-12 (usually 8 10) arranged symmetrically around a central mass of pigment like a daisy rosette	8 12
Duration of schizogony	48 hours	21 48 hours	72 hours	48 hours

	Benign Tertian	Malignant Tertian	Quartan	Oval Tertian
Form of gametocytes	Round or oval larger than a normal red cell	Crescentic or sausage shaped	Round oval about the same size as that of a normal red cell	Oval
Duration of sporogony	10 14 days.	8 11 days	18 1 days	10 14 days
Incubation period	14 18 days	9 12 days	18 21 days	14-18 days
Periodicity of fever	Usually tertian may be quotidian	Usually quotidian may be tertian	Usually quartan	Tertian
Duration of the febrile paroxysm.	Usually 6 8 hours	12 to 36 hour or more	Usually 4 6 hours	6 8 hours
Peripheral blood film	Shows all phases of both schizogony and sporogony multiple infection of red cell occasionally seen	Rings and crescents are the only forms seen except in very severe case Heavy multiple infection of red cells very characteristic	Shows all phases of both schizogony and sporogony Multiple infection of red cells very rare	Same as in benign tertian
Liability to relapse	Relapses may occur upto 3½ years from the time of the primary infection	Relapses less frequent than in benign or quartan infection may occur upto 9 month —1½ years from the time of primary infection	Relapses may occur for 6 19 year from the time of the primary infection	Short lived infection

parenchyma of the liver spleen pancreas In severe cases of malaria bilirubin is formed much in excess of what can pass through the liver cells into the bile ducts and the bowels and hence it circulates in the blood and stains the skin and mucous membranes yellow giving rise to a hæmolytic jaundice associated with an indirect or delayed direct van den Bergh reaction

A malarial paroxysm is therefore usually associated with hyper bilirubinæmia and urobilinæmia

Apart from the changes already described there is another very important change due to malarial infection namely the characteristic slaty pigmentation of the organs and tissues

The enormous amount of hæmozoin pigment liberated during schizogony is taken up by the large monocytes and the polymorphs of the peripheral blood Hence during the fever there is a leucocytosis with a relative increase of large monocytes and even of polymorphs many of which are pigmented The hæmozoin pigment is ultimately carried to be deposited in the reticuloendothelial cells of the splenic pulp Kupffer cells of the liver endothelial cells of the bone marrow adrenals lungs skin etc giving rise to the characteristic pigmentation

This pigment has also a toxic action on the endothelial cells of the capillaries and causes a cloudy swelling and degeneration of the phagocytic endothelial cells giving rise to hæmorrhage exudation and a blockage of the capillaries especially in *P falciparum* infection where schizogony occurs in the internal capillaries of various organs such as brain heart intestine spleen bone marrow and placenta The blockage of capillaries is also brought about by (1) numerous parasitised red cells clumped with one another and to the capillary endothelium (2) enormous numbers of mature schizonts (3) numerous liberated merozoites which are firm and cannot change their shape to conform to the lumen of the capillaries (4) clumps of free hæmozoin pigment (5) debris of parasites and of ruptured and hæmolysed red cells

Capillary blockage leads to ischæmia anoxæmia œdema and hæmorrhage associated with disturbances of function and gives rise to grave manifestations according to the organs affected and the site of capillary blockage

MORBID ANATOMY

Spleen In acute cases specially in *P falciparum* infection the spleen is slaty grey slightly or moderately enlarged and soft The cut surface shows a slaty grey pulp with marked engorgement and stretching of the capsule Histological examination shows marked congestion

4

PATHOLOGY

For a proper appreciation of the pathological changes that occur in malaria we must keep in mind the following facts regarding the erythrocytic cycle of the malaria parasite in the human host

1 Firstly the parasite grows inside the red cells at the expense of the hæmoglobin which is converted into a brown black pigment, *hæmozoin* It is an iron containing insoluble pigment and does not give the Prussian blue reaction

2 Secondly sporulation takes place in the peripheral blood but in the case of *P falciparum* almost exclusively in the capillaries of various internal organs

3 Thirdly with the rupture of the infected red cells there is a liberation into the peripheral and internal circulation of numerous merozoites a large amount of hæmozoin oxyhæmoglobin and disintegrated parasites and red cells

This process gives rise to a transient reaction like that of a protein shock associated with a chilly sensation vomiting rigor fall of blood pressure leucopenia thrombocytopenia diminution of red cells and altered coagulability of blood Abrami and Senevet have called it a *hæmoclastic shock* It is probable that the liberated merozoites or the debris of disintegrated red cells act as a foreign protein which produces the rigor and the fever The fever will show a tertian or quartan periodicity according to the cycle of the sporulation whether it occurs every 48 or 72 hours

During each paroxysm of fever there is not only a destruction of the infected red cells both erythrocytes and reticulocytes due to rupture of the mature schizonts but also a destruction of a large number of normal red cells probably due to the hæmolytic action of the hæmozoin pigment It is thus clear why repeated attacks of malarial paroxysm would produce a high grade anæmia of the hypochromic type As a result of increased blood destruction a large amount of hæmoglobin is set free in the circulation Under the activity of the reticuloendothelial cells chiefly the pulp cells of the spleen the Kupffer cells of the liver the hæmoglobin is split up into *hæmatin* and *globin* Hæmatin is converted into *hæmosiderin*—a yellow iron containing pigment giving the Prussian blue reaction and *hæmatoidin* which is an iron free pigment and is transformed into *bilirubin*—the bile pigment A part of the hæmosiderin is transported to the bone-marrow and utilised for the formation of hæmoglobin The rest is deposited in the cells of the reticuloendothelial system and also in the

Brain The brain may be slaty grey in colour Congestion and œdema with small punctiform hæmorrhages like flea bites may be seen in the cortex and the medulla

Microscopic examination shows capillaries to be filled with mature schizonts and sporulating forms of *P falciparum* and blocked by swelling of the endothelial cells with phagocytosed hæmozoin pigment and parasites

In chronic cases of malignant tertian malaria Durck has described the occurrence of subcortical malarial granulomas which may give rise to various psychical disorders Such granulomas consist of masses of proliferated neuroglial cells around an area of perivascular necrosis following blockage of the cerebral capillaries

Heart Fatty degeneration of the heart muscle may be seen in fatal cases of malignant tertian malaria Capillaries may be blocked by mature schizonts sporulating forms and free or phagocytosed hæmozoin pigment

Kidneys These show enlargement with an increase in bulk of the cortex Degenerative changes in the tubular epithelium are seen specially in untreated cases of quartan malaria Some workers have described malarial nephritis which is probably an allergic pheno menon due to sensitisation by foreign proteins from the parasite and tissue destruction in a previous attack

Suprarenals Degenerative and necrotic changes with hæmorrhage and thrombosis of the capsular vessels are seen in *P falciparum* infec tions Parasites and hæmozoin pigment are also seen in small numbers in the endothelial cells The lipoid content of the cortex may be reduced in *P falciparum* infection—causing asthenia and low blood pressure

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually a fortnight In a few cases it may be as short as 8 days

MODE OF ONSET The onset is usually sudden though in *P falciparum* infection it may be insidious like typhoid fever

PRODROMAL STAGE It is characterised by malaise headache bodyache chilly sensations nausea and anorexia

STAGE OF INVASION A typical malarial paroxysm consists of three stages *viz* (1) cold stage (2) hot stage and (3) sweating stage

Cold Stage The patient feels chilly and suddenly begins to shake involuntarily and passes into a stage of rigor even though covered with

parasitised red cells and free merozoites in the sinuses and the pulp and a large amount of brownish black hæmozoin pigment either scattered or engulfed by large mononuclear and reticuloendothelial cells

In chronic malaria the spleen is hard and markedly enlarged but not to such an extent as in chronic kala azar myeloid leukæmia and splenic anæmia On section it shows a homogeneous black surface interspersed with greyish white streaks Microscopic examination shows diffuse pigmentation and fibrosis atrophy of the malpighian bodies with collection of lymphoid cells around them marked thickening of the capsule with increase of fibrous tissue of the trabeculæ marked proliferation and inten e phagocytic activity of large mononuclear and endothelial cells which contain the malarial pigment and scanty parasitised red cells

Liver In acute cases it is dark grey in colour slightly or moderately enlarged due to marked dilatation and congestion of the hepatic capillaries and hyperplasia of the Kupffer s cells laden with hæmozoin pigment The hepatic cells may contain granules of hæmosiderin and occasionally bile pigment Cloudy swelling and fatty changes may be present specially in malignant tertian malaria In some cases varying degrees of centrilobular necrosis may be seen The hæmozoin pigment is never found in the liver cells

In chronic cases the liver may have a firm consistence due to certain amount of fibroblastic reaction and accumulation of mononuclear cells in the portal spaces probably due to the presence of the cryptozoic stage of the parasite Contrary to the common belief hepatic cirrhosis is never directly caused by chronic and repeated malarial infection

Intestine In acute cases specially in *P falciparum* infection the intestinal mucosa shows marked congestion and hæmorrhages The capillaries are blocked with red cells containing rings and mature schizonts of the malignant tertian parasite In chronic cases the mucous membrane has a slaty grey appearance

Bone marrow In the acute stage the colour is dark red due to congestion There is distinct reticuloendothelial hyperplasia with some hyperplasia of erythroblasts There may be associated hypoplasia of granular cells with probably relative increase of lymphocytes and plasma cells Numerous parasites and a large amount of pigment are seen engulfed in the endothelial cells of the marrow In the chronic stage the yellow marrow of the long bones changes to a chocolate brown colour

produced either by two generations of benign tertian parasites maturing on two successive days (*tertiana duplex*) or by two generations of *P falciparum* or by three generations of quartan parasites (*quartana triplex*) When two generations of quartan parasites mature on successive days the fever occurs on two successive days followed by a day of apyrexia (*quartana duplex*) When one febrile attack is prolonged so that the next paroxysm commences before the previous attack is terminated it is called *subintrant*

GENERAL APPEARANCE *Pallor and Anæmia* They are often present after a few paroxysms of fever The skin has developed a muddy colour due to the deposition of the malarial pigment (hæmozoin) in endothelial cells of the capillaries of the skin

Jaundice An icteric tinge of the skin and scleræ is often seen at an early stage of the malarial fever The icterus which is due to hyperbilirubinæmia may be slight or marked specially in malignant tertian malaria

Herpes Labialis The lips nose and ears frequently show herpetic eruptions following rigor specially in benign tertian infection

Cutaneous Eruptions Erythematous urticarial or even sometimes purpuric eruptions may appear during the febrile paroxysm

Alimentary Tract The tongue is coated with a brownish white fur Anorexia is marked Nausea retching and bilious vomiting are frequent due to the associated gastritis Diarrhœa or even dysentery due to catarrh in the lower bowel may be present and be so severe as to simulate cholera or bacillary dysentery

Spleen During an acute febrile paroxysm the spleen often enlarges and is palpable about a finger breadth below the costal margin soft and even tender The splenic enlargement may not however be clinically detected in many cases The patient may complain of pain in the splenic region due to stretching of the capsule by intense congestion Such a pain may simulate diaphragmatic pleurisy and lobar pneumonia In chronic malaria specially of the quartan type the spleen is moderately or greatly enlarged and hard (ague cake) In such cases the spleen is also very friable and thus liable to rupture even on slight injury Many deaths have resulted from blows or kicks over such a spleen

Liver The liver is usually slightly enlarged and tender during the febrile paroxysm With repeated attacks of malaria the liver is moderately enlarged and firm Marked enlargement of the liver is rare

plenty of warm bed clothes In children convulsions are frequently seen at this stage The stage usually lasts for half to one hour and is not so prominent in malignant tertian infection The pulse is full and rapid The temperature rises up gradually and he feels warm

Hot Stage The temperature often rises as high as 104°—106°F A temperature above 106°F (*hyperpyrexia*) is more common in benign than in malignant tertian infections Headache is present and often marked thirst is intense the eyes are congested and the skin is dry and hot Nausea and vomiting are frequently present in this stage The hot stage lasts for 1 4 hours

Sweating Stage It lasts for 2 4 hours The skin of the forehead and the whole body is bathed in perspiration which may be so profuse as to drench the bed clothes With sweating the temperature falls to the normal or even below and remains so for 1 3 days till the occurrence of the next paroxysm (*intermittent fever*) Febrile paroxysm may recur every third (*tertian fever*) (Fig 6) or every fourth day (*quartan fever*) (Fig 7) The *quotidian fever* (Fig 8) is

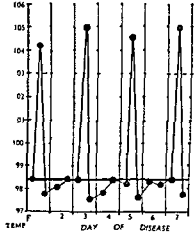


Fig 6 Tertian fever

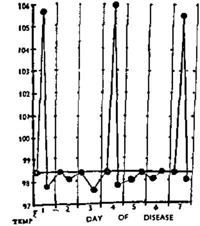


Fig 7 Quartan fever

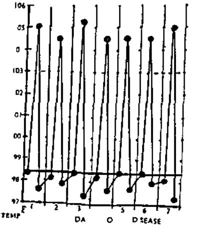


Fig 8 Quotidian fever

produced either by two generations of benign tertian parasites maturing on two successive days (*tertiana duplex*) or by two generations of *P falciparum* or by three generations of quartan parasites (*quartana tripl x*) When two generations of quartan parasite mature on successive days the fever occurs on two successive days followed by a day of apyrexia (*quartana duplex*) When one febrile attack is prolonged so that the next paroxysm commences before the previous attack is terminated it is called *subintrant*

GENERAL APPEARANCE *Pallor and Anæmia* They are often present after a few paroxysms of fever The skin has developed a muddy colour due to the deposition of the malarial pigment (hæmozoin) in endothelial cells of the capillaries of the skin

Jaundice An icteric tinge of the skin and scleræ is often seen at an early stage of the malarial fever The icterus which is due to hyperbilirubinæmia may be slight or marked specially in malignant tertian malaria

Herpes Labialis The lips nose and ears frequently show herpetic eruptions following rigor specially in benign tertian infection

Cutaneous Eruptions Erythematous urticarial or even sometimes purpuric eruptions may appear during the febrile paroxysm

Alimentary Tract The tongue is coated with a brownish white fur Anorexia is marked Nausea retching and bilious vomiting are frequent due to the associated gastritis Diarrhœa or even dysentery due to catarrh in the lower bowel may be present and be so severe as to simulate cholera or bacillary dysentery

Spleen During an acute febrile paroxysm the spleen often enlarges and is palpable about a finger breadth below the costal margin soft and even tender The splenic enlargement may not however be clinically detected in many cases The patient may complain of pain in the splenic region due to stretching of the capsule by intense congestion Such a pain may simulate diaphragmatic pleurisy and lobar pneumonia In chronic malaria specially of the quartan type the spleen is moderately or greatly enlarged and hard (ague cake) In such cases the spleen is also very friable and thus liable to rupture even on slight injury Many deaths have resulted from blows or kicks over such a spleen

Liver The liver is usually slightly enlarged and tender during the febrile paroxysm With repeated attacks of malaria the liver is moderately enlarged and firm Marked enlargement of the liver is rare

Circulatory System The pulse is rapid in proportion to the height of the temperature In malignant tertian cases however the pulse may be relatively slow a pulse rate of 90 100 may be found with a temperature of 104° 105°F

Blood Hypochromic anæmia of various degrees is a constant feature of the malarial fever In *P falciparum* infection the hæmoglobin percentage may be as low as 20 per cent and the red cells 1 5 millions per c mm Poikilocytosis anisocytosis polychromasia and occasionally macrocytosis may be seen The white cell count is variable Just before the febrile paroxysm there is a leucopenia but immediately after the febrile paroxysm of a primary attack specially of a malignant tertian infection there is leucocytosis which may be as high as 24 000 or even more with an increase of polymorphs Leucocytosis is also present in cases of malignant tertian infection associated with symptoms of dehydration due to vomiting and diarrhœa In chronic cases there is usually a slight or moderate leucopenia Increase of large monocytes which may be up to 20 per cent is almost a constant feature Hæmozoin pigment may be found in the polymorphs and the monocytes In most cases the malaria parasites are found in the peripheral blood There are certain biochemical changes in the blood of malaria patients in the acute stage such as (*a*) hyperbilirubinæmia (*b*) slight hypocholesterolæmia (*c*) diminution of the alkali reserve (*d*) slight increase of blood urea specially in severe cases of malignant tertian malaria.

Respiratory System Bronchitic manifestations are commonly found in malaria In many cases of *P falciparum* infection pneumonia and bronchopneumonia may occur as complications

Nervous System Various nervous manifestations *e g* headache delirium convulsions coma paralysis mental disturbances may be present according to the type and severity of the malarial infection Coma which is usually found in malignant tertian infection may occasionally occur in heavy benign tertian infections due to toxæmia as in any *other infectious fevers such as typhoid fever and pneumonia*

Urinary System The urine is copious and light coloured in the cold stage but scanty and high coloured during the hot stage An increased excretion of urobilin occurs during the attack Slight albuminuria is not uncommon during the febrile stage

SPECIAL CLINICAL FEATURES OF BENIGN TERTIAN MALARIA

Incubation Period Usually a fortnight

Prodromal Stage Usually present

Fever It is usually of sudden onset but may be insidious in a few cases with slight irregular fever specially in children Hyper pyrexia a temperature of 106°F or over is more common in benign tertian than in malignant tertian malaria

Type It is usually intermittent and quotidian later tertian The initial attack in a nonimmune subject may take a remittent course and there may be a daily rise of temperature Tertian periodicity (Fig 9) continues for 2 to 3 weeks if left untreated

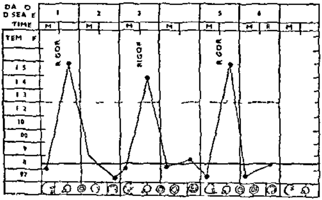


FIG 9 Temperature chart of benign tertian malaria showing the relation of temperature to the various phases of schizogony of the parasite

Character The cold hot and sweating stage are all well marked

Duration Each paroxysm lasts usually from 5 to 8 hours It continues for 2 to 3 weeks if left untreated

Relapse Very common and usually milder than the primary attack Relapses may continue for a long period Inspite of proper treatment in most cases the fever returns after 2 8 weeks If adequate treatment is not given these recurrences occur between 8 13 weeks or even upto 4 years (Manson) In most cases relapses cease in 2 years

Spleen It is often palpable during the paroxysm and gradually enlarges with the recurrence of the febrile attacks

Anæmia It becomes more pronounced as the disease tends to become chronic

SPECIAL CLINICAL FEATURES OF QUARTAN MALARIA The infection is the least common of all The incubation period is three weeks The periodicity of the paroxysm is quartan *i e* it comes every 4th

day and is very regular (Fig 10) The temperature is usually above 104°F The paroxysm is of shorter duration usually 4 to 6 hours Double infection with two broods of parasites giving rise to *quartana duplex* fever is occasionally seen Triple quartan infection giving rise to quotidian fever is rare The parasites are rather scanty in the peripheral blood Though the febrile attack is very easily checked by quinine the infection may persist for a long time giving rise to relapses A case is on record where such relapses occurred over a period of 19 years It does not produce cachexia very readily But quartan malaria is liable to be associated with nephrosis in many cases due to *the long continued action of malarial toxins on the kidneys*

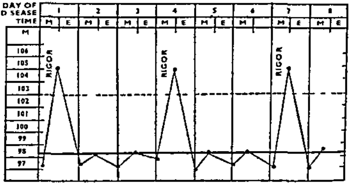


FIG 10 Temperature chart of quartan malaria

SPECIAL CLINICAL FEATURES OF PLASMODIUM OVALE INFECTION The infection is comparatively mild as seen in different parts of West and Central Africa The rigors and fever having a tertian periodicity and associated with bone pains invariably come on in the evening instead of in the morning as in other types of malaria Abdominal pain referred to the appendicular region and rheumatic pains specially in the lumbar region are characteristic features

SPECIAL CLINICAL FEATURES OF MALIGNANT TERTIAN MALARIA This is the most important and serious type of malaria because it is responsible for most of the severe epidemics The incubation period is 5 10 days The temperature curve associated with this infection is variable (Figs 11 & 12) and seldom conforms to the typical character of malarial fever The onset may be insidious in many cases simulating typhoid fever (typhoid remittent) At the beginning of the infection the fever is usually intermittent but later on it may be remittent

in a good percentage of cases showing even a double rise Tertian periodicity is less common than quotidian The rigor and sweating

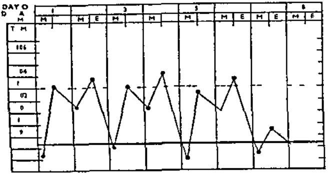


FIG 11 Temperature chart of malignant tertian malaria

stages are less marked and the febrile stage may be prolonged more than 24 hours with overlapping of the paroxysms due to the presence

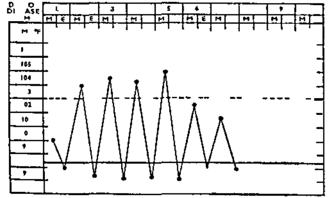


FIG 12 Temperature chart of malignant tertian malaria (quotidian type)

of two broods of parasites one maturing somewhat later than the other Spleen is usually enlarged one or two fingers breadth below the costal margin and is rather firm Symptoms like bilious vomiting purging jaundice severe headache delirium coma etc are more marked and much more common in this infection than in benign tertian or quartan malaria In some cases of so called bilious remittent type epigastric pain persistent bilious vomiting marked jaundice due to

hyperbilirubinæmia occasionally bilious diarrhœa bile stained urine (urobilinuria) and a delayed direct van den Bergh reaction are the characteristic features In a few others the jaundice appears early the liver is slightly enlarged and tender The van den Bergh reaction is biphasic Hæmorrhages from the various mucous membranes and into the skin may occur The malignant tertian malaria is relatively less liable to relapse The whole course of the disease is shorter and sharper than that of benign tertian or quartan infection ending either in death or clinical cure under proper treatment

It produces a rapidly developing hæmolytic anæmia and marked cachexia In about 4-6 weeks of a primary attack in some cases a macrocytic anæmia may be seen The rings and the crescents are the only forms seen in the peripheral blood In severe and fatal cases schizonts may however appear in the peripheral blood

The fever which requires immediate treatment responds more readily to quinine or mepacrine than in benign tertian or quartan infection Relapses occur frequently 4 6 weeks after the first attack and are rare after 9 months to 1 year after the endemic area is left

PERNICIOUS MANIFESTATIONS Malignant tertian infection whether in the primary attack or in course of subsequent relapses is very liable to produce grave or pernicious clinical manifestations due to the blockage of the internal capillaries of various organs by numerous clumps of infected red cells sporulating parasites and an enormous amount of hæmozoin pigment The nature of these manifestations would vary according to the site of capillary blockage The pernicious manifestations may be classified as follows

1 *Cerebral Type* In this type cerebral or nervous symptoms like delirium mania drowsiness coma convulsions hyperpyrexia aphasia hemiplegia paraplegia bulbar paralysis amblyopia optic neuritis and retinal hæmorrhage may appear within 48 or 72 hours of the onset of the disease

According to the predominance of one or more of these symptoms the cerebral malaria may be further subdivided into (*a*) *comatose* (*b*) *hyperpyrexial* (*c*) *encephalitic* (*d*) *epileptiform* and (*e*) *meningitic* types

In case where delirium and coma are the most pronounced features the temperature is generally high but probably may not rise above 104° or 105°F In about 20 per cent of cases the skin temperature may be subnormal Premonitory symptoms like muscular twitchings talkativeness drowsiness or slight muttering delirium may

precede the attack or the attack may appear with dramatic suddenness and carry away the patient before any treatment can be adopted

2 *Algid Type* It is characterised by the presence of cold and clammy skin associated with collapse and an imperceptible pulse due to an acute peripheral failure *Surface* temperature may be low but the *internal* temperature is usually high The clinical manifestations may be described under the following heads

(a) *Gastric form* Epigastric pain and persistent vomiting are the chief features Hæmatemesis may occur in some cases

(b) *Choleraic form* In this form vomiting and purging are the prominent features (Usually vomiting precedes purging The patient passes numerous loose bile stained stools) Loss of fluid may be so great that the patient may have pinched up cholera facies cramps and suppression of urine Collapse sets in and ends in death This form is very deceptive as it closely simulates cholera Correct diagnosis which is very essential can be made with certainty only by blood examination

(c) *Dysenteric form* In this form the stools contain mucus and occasionally blood simulating those of acute bacillary dysentery Surface temperature is generally high in these cases

3 *Hæmorrhagic Type* In this form sudden hæmorrhage from stomach or bowels takes place Hæmorrhage may also occur from nose and mouth and in conjunctive and in the skin as multiple petechiæ Perhaps it also occurs in the peritoneal cavity producing symptoms of peritonitis and appendicitis Hæmorrhage in the brain and spinal cord may also occasionally occur Bleeding from the genito urinary passages may sometimes be found Correct diagnosis is possible only by blood examination The possibility of such sudden hæmorrhages from stomach or bowels in malarial infection should be borne in mind

The choleraic and hæmorrhagic symptoms in the algid form of malaria may be due to blockage of the vessels of the intestinal mucosa with parasites

Syncopal Type Sudden death from cardiac failure due to blockage of the coronary capillaries by sporulating parasites or toxic fatty degeneration of myocardium is not uncommon during the sweating stage of defervescence in some cases of malignant tertian malaria.

Respiratory Type Signs of bronchitis and occasionally of broncho pneumonia and pneumonia are predominant in some cases of malignant malaria Pneumonia and broncho-pneumonia are merely

superadded to the malarial infection and there is no proof that they are caused by the malaria parasites

Mixed Infections Very often two kinds of parasites may be found in the blood of a patient at the same time Generally benign tertian and malignant tertian are found together Mixed infection produces more severe symptoms than single infection The importance of mixed infections is that the co existence of malignant tertian infection may sometimes be overlooked in cases in which benign tertian parasites have been found Cases are on record where repeated blood examinations failed to reveal malignant tertian parasites but showed plenty of benign tertian and when that blood was injected as a therapeutic measure it produced malignant tertian infection and caused fatalities Detection of mixed infections is also very important from the point of view of treatment

Latent Malaria Persons who had previously suffered from malaria or who had lived in malarious places may for a long time harbour malaria parasites gametocytes more often than schizont in their blood without any definite symptoms Some of them however may show weakness anæmia and varying degrees of splenomegaly The multiplication of the parasites is kept in check by the natural or acquired immunity of the individual and thus the pyrogenic threshold is not reached

In many of these cases after a varying period of latency the infection may suddenly flare up under conditions of lowered resistance brought about by exposure to cold rains and the sun heavy exertion injuries childbirth surgical operations and even a preventive inoculation

Malaria in Childhood Children are very susceptible to a malarial infection which may be acquired immediately after birth or rarely be congenital due to placental infection The clinical manifestations are often misleading Fever which is not high comes on at night and is often missed Shivering and sweating are uncommon Symptoms of meningism with convulsions vomiting and diarrhœa are frequently seen The child may be apathetic and lethargic or even comatose Progressive hypochromic anæmia and a rapid enlargement of the spleen and liver are common

Artificial Malaria Malaria has been induced in man by the bite of a mosquito infected with *P vivax* by the subcutaneous injection of a normal *saline suspension of the sporozoites* or by the intra

muscular or intravenous injection of 2 5 c cm of defibrinated blood containing benign tertian parasites for the treatment of neuro syphilitic conditions such as dementia paralytica and tabes dorsalis From a study of such experimentally induced primary benign tertian malaria it has been shown that (i) the incubation period varies from 7 to 23 days (ii) the clinical course consists of three stages (a) initial stage (b) the stage of full development and (c) the terminal stage Recently *Plasmodium knowlesi* has been used for this purpose Some workers were bold enough to use *Plasmodium falciparum* but this is definitely risky in view of the uncertain course of this infection

In the initial stage it is impossible to find the parasites particularly *P vivax* and the fever is irregularly remittent and lasts for a week or more after which it is intermittent Rigor is absent In the stage of development the fever is quotidian in type associated with a daily rigor and lasting for about 10 days In the terminal stage the fever has the typical tertian periodicity with rigor every 48 hours In case of relapse or re infection the first two stages are absent and the fever shows a typical tertian periodicity

It is also interesting to note that artificial malaria (trophozoite inoculated malaria) is easily curable by anti malarial remedies such as quinine and mepacrine Relapses also are very rare

COMPLICATIONS

1 Development of cerebral symptoms such as hyperpyrexia delirium coma convulsions paralysis aphasia amblyopia and neuritis
2 Dysentery and choleraic diarrhœa
3 Syncopal cardiac failure
4 Hæmorrhages from and into the various organs and tissues
5 Pneumonia and broncho pneumonia
6 Severe hæmolytic jaundice due to excessive blood destruction
7 Blackwater fever
8 Abortion in pregnant women
9 Orchitis
10 Mastitis
11 Nephrosis specially in chronic quartan malaria

SEQUELÆ

1 Relapse
2 Varying grades of hypochromic anæmia with or without post malarial œdema
3 Blackwater fever

4 Pulmonary tuberculosis a common sequel in cachectic cases

5 Malarial cachexia characterised by puffy face stunted growth in children asthenia sallow complexion marked anæmia œdema of the limbs enlargement of spleen and liver digestive disturbances low bloodpressure and occasionally anasarca

6 Sterility in females and impotency in males

7 Occasionally dry gangrene of the toes due to thrombotic changes

8 Disturbances of speech such as aphasia dysphasia

9 Polyneuritis

10 Melancholia and mania

11 Keratitis and iritis

PROGNOSIS

The prognosis in malaria usually depends on the type of infection its severity and the possibility of an early diagnosis and immediate treatment Cases of heavy malignant tertian infection with pernicious manifestations have a serious prognosis and the mortality may be as high as 40 per cent inspite of the most prompt and energetic treatment There are however other factors which influence the prognosis such as age sex race individual constitution and associated diseases A malarial attack is more severe in children than in adults Women specially in pregnant state show more serious symptoms than men Malaria is an important cause of abortion miscarriage and still birth in the tropics Europeans who have not been acclimatised to the tropical conditions are more liable to severe malarial attacks than the local residents who have acquired a certain degree of immunity Under debilitating conditions such as malnutrition hookworm anæmia diabetes mellitus chronic nephritis pulmonary tuberculosis and chronic dysentery a malarial attack even due to a benign tertian parasite may turn out to be fatal

DIAGNOSIS

Considering that an early and accurate diagnosis is quite possible in this disease a delay in diagnosis or an erroneous diagnosis which may cost a patient s life is not justified The diagnosis should be based on a correlation of the following clinical and laboratory data

CLINICAL DATA 1 History of febrile attacks off and on and history of living in a malarious place or recently visiting such a place

2 Sudden onset of high fever with a temperature of 104°F or more

3 Daily paroxysm of fever coming in the forenoon or early afternoon with rigor and passing off with sweating

4 Typical tertian or quartan periodicity of the paroxysms

5 Presence of pallor and anæmia

7 Early appearance of one or more of the following

(a) Hyperpyrexia (b) Delirium coma convulsions and paralysis (c) Bilious vomiting and diarrhœa (d) Icteric tinge of the conjunctive (e) Anæmia (f) Hæmaturia or hæmoglobinuria (g) Herpes labialis

8 Early appearance of a palpable spleen (in 60 per cent) with or without tenderness or of an enlarged liver (33 per cent)

9 A rapid pulse rate out of proportion to the height of temperature We have however seen a relatively slow pulse rate in some cases of malignant tertian infection

LABORATORY DATA 1 *Blood Examination* The blood of a suspected case of malaria should be examined for the presence of malaria parasites specially before the stage of rigor and before the administration of any antimalarial drugs The usual method employed for the purpose is an examination of thin and thick films of blood Unless several thin films and a thick film are carefully examined malaria parasites are detected only in 58 per cent of cases Hence one negative report does not exclude the possibility of malaria Detection of rings growing trophozoites or schizonts clinches the diagnosis of malaria but such a diagnosis is not justified on the presence of gametocytes alone In cases where parasites are not found presence of a monocytosis (15 20 per cent) and hæmozoin in the leucocytes is suggestive of malarial infection Thin film is usually stained with any of the Romanowsky stains Leishman s stain being most commonly used The value of a thick film method is obvious a much larger quantity of blood is examined within a shorter time facilitating diagnosis of scanty infection The disadvantage of thick film is that the species of malaria parasite cannot be identified with certainty

Methods of staining the thick film —

Method I The film is dried and then dehæmoglobinised with a special solution containing 4 parts of 2 5 per cent solution of glacial acetic acid and 1 part of [illegible] per cent solution of crystalline tartaric acid The film is subsequently stained with any of the Romanowsky stains

Method II Method of Field (1941) Two solutions are required for this stain—methylene blue and azur I and eosin both in isotonic solution adjusted to pH 6 6 Isotonicity and correct pH are maintained by the amount and proportions of the acid and alkaline phosphates which the stains contain

Solution (A)

Methylene blue	0 8 gramme
Azure I	0 5
Disodium hydrogen phosphate (anhydrous)	5 0 grammes
Potassium dihydrogen phosphate (anhydrous)	6 25
Distilled water	500 c.cm

Solution (B)

Eosin	1 0 gramme
Disodium hydrogen phosphate (anhydrous)	5 0 grammes
Potassium dihydrogen phosphate (anhydrous)	6 25
Distilled water	500 c cm.

Technique of Field's Stain —

(1) Dried thick film is dipped in Solution (A) for 3 seconds
(2) The film is then washed for 3 seconds by gentle motion in a jar of clean water
(3) The film is next dipped in Solution (B) for 2 seconds
(4) The film is subsequently washed again in water for 2 seconds
(5) If necessary the film may require a second dip for one second in Solution (A) with a final wash in water
(6) *The film is thus ready for examination within half a minute*

Field's method is quicker simpler and more suitable for practical use Method I however facilitates detailed morphological studies

2 *Examination of Sternal or Splenic Puncture Material* Method of examination by puncture may be adopted with success in cases of atypical and chronic malaria specially due to *P vivax* Stained films from such material would show hæmozoin pigment and parasites Some workers claim to have found parasites in marrow films in cases of acute or latent malaria where thick film preparations of peripheral blood gave persistently negative results This is also our experience

3 *Cultivation of Blood for Malaria Parasites* Hæmoculture according to modified Bass technique is of value where no malaria parasites have been detected on examination of thick and thin films On culture the first schizogony cycle is usually seen rarely the second or third cycle

4 *Serum Tests* Complement fixation test Henry's flocculation test and intradermal tests have been described but these are seldom used in clinical practice

DIFFERENTIAL DIAGNOSIS

The manifestations of malaria are protean enough to simulate many diseases amongst which the following are common

Enteric group of fevers kala azar pulmonary tuberculosis *Esch*

coli infection pneumonia influenza cerebrospinal meningitis heat stroke amœbiasis with liver abscess cholera bacillary dysentery

ACUTE MALARIA has to be distinguished from the following

1 *Enteric Group of Fevers* (*a*) Insidious onset with intense headache (*b*) Relative bradycardia with occasional dicrotism (*c*) Presence of rose spots over the abdomen and chest (*d*) Slight enlargement of the spleen and liver which are soft (*e*) Leucopenia with lymphocytosis (*f*) Positive blood culture and Widal's test

2 *Acute Kala a ar* (*a*) Typhoid like onset (*b*) Presence of double rise in the temperature chart (*c*) Rigor and sweating not common (*d*) Presence of clean tongue and good appetite (*e*) Presence of a slightly or moderately enlarged soft spleen and also of a slightly enlarged liver (*f*) Progressive leucopenia with neutropenia and lymphocytosis (*g*) Positive complement fixation test and Chopra's test (*h*) Positive flagellate culture (*i*) Presence of *L dono ani* in sternal smear

3 *Cerebrospinal Meningitis* (*a*) Lateral decubitus associated with severe headache and signs of meningeal irritation (*b*) Presence of relative bradycardia (*c*) Presence of high leucocytosis (*d*) Turbid or frankly purulent cerebrospinal fluid on lumbar puncture (*e*) Presence of *Neisseria meningitidis* on smear and on culture of the cerebro spinal fluid

It is rather difficult to distinguish at times cerebrospinal meningitis from cerebral malaria on the basis of clinical features In every case of fever with a very early appearance of cerebral symptoms an examination of the blood for malaria parasites and in their absence a lumbar puncture to exclude cerebrospinal meningitis are essential

4 *Lobar Pneumonia* (*a*) Pain referred to the affected side of the chest (*b*) Shallow and rapid respirations with alteration of the pulse respiration ratio from 3 1 to 2 1 (*c*) Rusty sputum (*d*) Localising lung signs such as diminished movement impaired resonance tubular breathing and crepitations (*e*) Leucocytosis

5 *Influenza* (*a*) Presence of naso pharyngeal catarrh and bronchitic signs (*b*) Relative bradycardia

6 *Dengue* (*Pre eruptive Stage*) (*a*) Occurrence of epidemics (*b*) Sudden onset with headache back ache retro orbital soreness and severe pains in joints and muscles (*c*) Generalised flush over the body (initial rash) (*d*) Relative bradycardia (*e*) Leucopenia

7 *Cholera* (*a*) Occurrence of epidemics (*b*) Usually afebrile axillary temperature often subnormal (*c*) Profuse diarrhœa precedes

vomiting whereas in algid malaria vomiting precedes diarrhœa (*d*) Absence of bile in the vomit and stools (*e*) High leucocytosis (*f*) Presence of actively motile *V cholera* in a hanging drop preparation of the stools confirmed later on by culture

8 *Acute Bacillary Dysentery* (*a*) Frequent passage of pink stools associated with griping and tenesmus (*b*) Presence of abdominal rigidity and tenderness specially over the descending and sigmoid colon (*c*) Vomiting less marked (*d*) Leucocytosis (*e*) Presence of discrete red cells numerous pus cells and macrophages in the stools

9 *Esch coli Infection of the Urinary Tract* (*a*) Spiky temperature chart (*b*) Comparative sense of well being inspite of the high temperature (*c*) Clean tongue (*d*) Frequency of micturition with pain in the loins (*e*) Turbidity and fishy odour of urine (*f*) Presence of numerous pus cells in urine (*g*) Culture of a catheter specimen of urine showing *Esch coli*

10 *Pulmonary Tuberculosis (Pneumonic or Broncho pneumonic)* (*a*) History of pleurisy pleural effusion and unexplained hæmoptysis (*b*) History of contact with an infective case of pulmonary tuberculosis in or outside the family (*c*) Presence of old tuberculous lymph adenitis specially in the neck (*d*) Appropriate physical signs in the lungs specially in the upper lobes (*e*) Positive sputum (*f*) Presence of parenchymal infiltrations as shown by a good skiagram

11 *Amœbic Liver Abscess* It is often mistaken for malaria It may be distinguished from the latter by (*a*) History of dysentery or diarrhœa (*b*) A sallow complexion of the face with a yellowish tint (*c*) Occurrence of sweating during sleeping hours without any relation to the height of temperature (*d*) Localised swelling pain and tenderness in the hepatic area (*e*) Pain over the right shoulder (*f*) Enlargement of the liver downwards and less commonly upwards The liver is more enlarged than the spleen (*g*) Leucocytosis though not invariable associated with a moderate increase of polymorphs and normal count of large monocytes (*h*) Presence of *E histolytica* cysts in stools is suggestive (*i*) Response to emetine therapy

12 *Weil's Disease* (*a*) Appearance of jaundice on the 3rd to 5th day of the disease (*b*) Gradual subsidence of temperature with the appearance of jaundice (*c*) Presence of conjunctivitis causing the pink eyes (*d*) Hæmorrhages into the skin and from the mucous membranes (*e*) Slight or moderately enlarged tender liver with little or no enlargement of the spleen (*f*) Proteinuria with hyaline and granular casts in the urine (*g*) Detection of *L icterohæmorrhagiæ* on

inoculation of the patient's blood into the peritoneal cavity of a guinea pig (*h*) Positive agglutination test

13 *Acute Bacterial Endocarditis* (*a*) Presence of marked toxæmia pallor and anæmia (*b*) Appearance of murmurs with slight cardiac enlargement (*c*) Petechial rash common (*d*) Occurrence of embolic phenomena in various organs and tissues (*e*) Leucocytosis (*f*) Positive hæmoculture

14 *Acute Filarial Lymphangitis* (*a*) Periodic attacks of fever sometimes corresponding to the phasic cycle of the moon (*b*) Appearance of the febrile paroxysm with chill and rigor usually at midnight (*c*) Enlargement of the affected lymphnodes associated with a redness of the overlying skin and painful cordlike swelling of the lymphatics (*d*) Neutrophilic leucocytosis and eosinophilia in some cases (*e*) Presence of micro-filariæ in the blood

CHRONIC MALARIA has to be diagnosed from the following

1 *Chronic Kala a ar* (*a*) Afebrile periods shorter than in malaria the course of the disease is usually 1 2 years (less than that of malaria) (*b*) Presence of double rise in the temperature chart during the febrile period (*c*) Pallor and anæmia more marked (*d*) Presence of clean tongue with good appetite (*e*) Splenic enlargement is out of proportion to the duration of the fever and firm to the feel (*f*) Liver is moderately enlarged and soft Hepatic enlargement is more than in malaria (*g*) Leucopenia progressive and more marked than in malaria (*h*) Detection of *L dono ani* in the sternal puncture material (*i*) Positive complement fixation test Chopra's test and formol gel or aldehyde reaction (*j*) Positive flagellate culture

2 *Tropical Splenomegaly* (see under Tropical Splenomegaly)

3 *Splenic Anæmia* (*Banti's Syndrome*) (*a*) Usually a long afebrile course with an enlarged spleen of 10 12 years (*b*) History of recurrent hæmatemesis and melæna (*c*) Splenomegaly and anæmia more marked (*d*) Evidences of hepatic cirrhosis such as prominent abdominal veins ascites Sometimes a hard and irregular liver may be palpable (*e*) No response to antimalarial therapy

4 *Chronic Myelogenous Leukæmia* (*a*) History of slight febrile episodes (*b*) Splenic enlargement is more marked than in chronic malaria of the same duration (*c*) Hæmorrhages into the skin and from mucous membranes may occur (*d*) Presence of sternal tenderness (*e*) A very high leucocytosis with relative or absolute increase of immature granular cells in the blood

5 *Hodgkin's Disease* (*a*) Marked enlargement of the lymph nodes specially of the neck (*b*) Firm elastic painless and discrete character of the enlarged glands (*c*) Occurrence of the Pel Ebstein type of fever (*d*) Splenic enlargement is moderate and not marked as in chronic malaria Sometimes the spleen has an irregular feel (*e*) Moderate leucocytosis with slight eosinophilia in most cases

6 *Portal Cirrhosis* (*a*) Usually afebrile unless associated with secondary infections or a rapidly progressive course (*b*) Presence of the characteristic hepatic facies—thin face sallow complexion dilated venules on the nose and cheeks and the icteric watery conjunctivæ (*c*) History of hæmatemesis melæna and of bleeding piles may be present (*d*) Splenic enlargement is slight or moderate (*e*) Presence of ascites with prominent veins on chest and abdomen with the flow of blood from below upwards

TREATMENT

The treatment of malaria consists in (*a*) the management of primary or acute attacks (*b*) control of relapses (*c*) eradication of a chronic infection and (*d*) prevention of malaria

The management of a primary or acute attack of malaria is based on the adoption of (*i*) general (*ii*) specific and (*iii*) symptomatic measures

GENERAL MANAGEMENT

During the febrile stage the patient is kept in bed to ensure rest Warmth is maintained in the cold stage by the use of blankets and hot water bottles A combination of diaphoretics and diuretics is used to promote heat loss and elimination of toxins It is also essential to maintain the alkali reserve of the blood which is often reduced in the acute attacks of malaria so that the action of quinine may be reinforced Hence the following mixture may be given every 4 6 hours

R/

Potassii acetatis	gr x
Sodii citratis	gr xx
Syrupi aurantii	dr ½
Aquæ ad	oz i

Fiat mistura

Immediately after the sweating stage care should be taken to change the wet clothing

A regular action of the bowels hould be maintained except in the

algid cases by a dose of calomel gr iii at night followed by a morning dose of an ounce of saturated solution of magnesium sulphate

During convalescence bed rest should be continued for a week after the defervescence of fever General health of the patient should be improved by adequate treatment and diet A tonic and hæmatinic mixture may be advised to improve the blood condition and to promote the antibody formation A tonic such as Eastons Syrup (Syrupus Ferriphosphatis cum quinina et strychnina B P) one tea spoonful diluted with water may be taken twice daily after meals The following prescription is also helpful

R/

Quininæ sulphatis	gr iii
Ferri sulphatis	gr v
Magnesii sulphatis	gr xx
Liquoris arsenicalis	m iii
Acidi sulphurici diluti	m v
Syrupi limonis	m xxx
Aquæ menthæ piperitæ ad	oz i

Fiat mistura

One dose should be taken three times daily after food for a fortnight

Diet During the acute stage it is desirable to withhold all solid food as unpleasant symptoms may follow if the patient gets a febrile paroxysm on full stomach Adequate amount of fluids such as barley water plain water glucose water lemonade should be given till the temperature comes to normal During convalescence appetite is the best guide and a liberal diet adequate in calories and vitamins should be given

SPECIFIC TREATMENT

Quinine which until recently was the sheet anchor in the treatment of malaria still remains a potent drug but the newer synthetic anti malarial drugs like mepacrine proguanil chloroquine plasmoquine etc are being increasingly used in treatment

QUININE AND ITS ALLIES QUININE Sulphate hydrochloride dihydrochloride and dihydrobromid are the common salts of quinine which are used in the treatment of malaria Quinine sulphate which is the cheapest is as effective as the more expensive salts and for routine treatment this is the drug which is most extensively used

Whatever preparation of quinine is used quinine circulates in the blood as quinine base which is the most effective agent against malaria parasites

The following table shows the solubility and the quinine content of these salts —

Salts	Solubility in water	Content of quinine base (per cent.)
Sulphate	1 in 800	73 5
Hydrochloride	1 in 40	81 7
Dihydrochloride	1 in 1	81 6
Dihydrobromide	1 in 1	60 0
Ethyl carbonate	slightly soluble	87 0
Dihydrochloride of quinine and urea ...	1 in 7	59 2

Action of Quinine Soluble or insoluble salts of quinine when given per mouth are almost equally rapidly absorbed chiefly from the duodenum and small intestine In the duodenum the alkaline salts throw down the quinine alkaloid which is absorbed into the blood and circulates as a quinine base in a dilution not more than 1 in 100 000 Most of the quinine given in one dose is absorbed within six hours and is found in the urine within 15 minutes and disappears from it in about 72 hours by whichever route it may be given Quinine taken even in small doses is also excreted through the milk of nursing women Its presence in the urine can be tested by taking 5 c cm of urine boiling filtering the albumen if present and adding a few drops of Tanret Mayer s reagent which will give a precipitate Quinine being absorbed circulates in blood for a very short time two thirds of it is deposited and destroyed in the tissues *e g* liver spleen brain etc. and the rest is excreted in the urine Effective blood concentration is estimated to be 5 mg per litre of blood Its effect begins within half an hour and lasts for more than six hours

The exact mode of action of quinine on malaria parasites is not well understood Quinine acts on these parasites by mobilisation of the defensive mechanisms of the body through the reticuloendothelial system such as phagocytosis and antibody formation

Quinine is effective both as a suppressive drug and in the control of clinical attacks Its primary action is schizonticidal Quinine has some action on the gametocytes of *P vivax* and *P malariæ* but is ineffective against the gametocytes of *P falciparum* It has no action on sporozoites and pre and exo-erythrocytic forms

Mode of Administration Oral method Quinine is generally

given by mouth as the method of choice but it can be given intra muscularly or intravenously if necessary For routine administration the most reliable method is to give quinine sulphate in solution by mouth preferably preceded ½ an hour before by an alkalinising mixture When given by mouth it is usually absorbed at same rate as when given by intramuscular injection Quinine sulphate may be prescribed in solution by the addition of a dilute mineral acid such as dilute sulphuric acid (B P) in m i dose per grain of the salt or citric acid in gr iii dose per grain of the salt Many of the symptoms of cinchonism such as tinnitus giddiness insomnia can be averted by adding dilute hydrobromic acid in m i dose per grain of the salt instead of sulphuric acid or citric acid If the patient refuses to take it per mouth for its bitter taste it can be given in cachets in capsules in tablets (preferably non sugar coated) or in freshly prepared pills In such cases each dose should be followed by a drink of lime juice in water If the patient cannot retain anything in the stomach due to gastric irritability quinine should be given parenterally

Intramuscular method As quinine is equally absorbed when given by mouth this method cannot be regarded as the method of choice Some claim a quicker and more effective action but this is questionable It has been found that with intramuscular injections quinine appears in the urine in about an hour while with the oral method it appears in the urine in about 15 minutes A 30 to 40 per cent solution of quinine dihydrochloride is used and a dose of 7½ to 10 grains dissolved in 2 c cm of normal saline is injected into the gluteal muscles over the upper and outer quadrant of the buttock with the strictest asepsis The intramuscular injection of quinine should not be repeated more than twice but should be replaced by the oral administration of quinine after the third injection There is an objection to the intramuscular administration of quinine dihydrochloride which is too acid (pH about 3 5) and therefore likely to cause pain necrosis and sepsis

Indications 1 Presence of urgent and severe manifestations such as hyperpyrexia coma convulsions and delirium in *P falciparum* infections

2 Presence of persistent nausea vomiting and diarrhœa which are likely to interfere with the absorption of quinine

3 Reluctance on the part of the patient to take quinine by mouth for its bitter taste

Advantages 1 The physician is sure that his patient has got the prescribed quantity which cannot be tampered with

2 Quinine is sure to be absorbed as there is no chance of its being vomited out and under certain conditions its action will be more rapid when given by mouth

Disadvantages 1 It is a painful procedure

2 In some cases it results in necrosis of the tissues abscess formation injury to the vessels and nerves tetanus gas gangrene etc It is not desirable and is seldom necessary to give more than 3 injections at an interval of 12 to 24 hours

Intravenous method 7½ grains of quinine dihydrochloride dissolved in 50 c cm of warm sterilised normal saline is injected To avoid shock the injection of a freshly prepared solution is given at the rate of 2 c cm per minute very slowly with the patient in the recumbent and adrenaline should be kept ready at hand but the latter should never be mixed with the quinine solution Preferably 10 grains of quinine bihydrochloride may be given in ½ 1 pint of normal saline by intravenous drip As a rule intravenous injection of quinine rarely need be repeated but if the condition of the patient has not improved this may be repeated after 8 12 hours

Indications 1 Malignant tertian infection producing pernicious symptoms

2 Heavy infection showing numerous parasites in the peripheral blood

Advantages There is neither any delay in absorption nor any chance of non absorption and the drug reaches the blood at once

Disadvantages 1 Rapid fall of bloodpressure which may be so marked as to cause collapse or syncope

2 95 per cent of the drug disappears from the blood within 5 minutes of the intravenous injection so its action though rapid is not sustained

3 In cases of quinine intolerance it may cause death

4 Phlebitis and thrombophlebitis—may rarely occur

Time of Oral Administration of Quinine Some authorities to be sure of its absorption recommend that the bowels should be opened with a dose of saline purgative before giving quinine Absorption is rather slower when quinine is taken on a full stomach or when constipation exists Some suggest that it is better not to administer quinine during the cold or hot stage but to give it when the patient begins to perspire with the idea that quinine given during the rigor or hot stage aggravates the headache and general distress Others advocate administration of quinine 2 3 hours before the expected paroxysm so that the drug may

be in maximum concentration in blood at a time when the young parasites are found in abundance in the blood stream and when they are in the least resistant form i e the *amœboid* form These however do not make much difference and in practice quinine ought to be given as soon as the diagnosis is made and it should be continued orally at 6 8 hourly intervals

Dosage of Quinine It is not possible and it will be unwise to lay down any definite rules regarding the dosage to be employed but it must be remembered that large heavy doses of quinine are not more effective than moderate doses or repeated small doses 20 grains in 24 hours may be t ken as the full dose for average Indian adults Children require relatively higher dose and tolerate the drug exceptionally well 12 to 15 grains for children between 5 and 10 years 7 to 10 grains for children between 2 and 5 years 4 to 6 grains for children of half to 2 years under 6 months 3 grains in 24 hours

Length of Treatment The hort course of quinine therapy is now preferred to the long course advocated previously

Short cours 20 grains of quinine sulphate or dihydro hloride are given daily by mouth till the temperature is normal Then a daily dose of 15 grains is continued till a seven day course is completed If there is no relapse no more quinine need be given but if there be relapse the whole course of treatment is repeated It must be realised that frequency and severity of relapses depend on the degree of immunity which the infected host possesses naturally or acquires through previous attacks of malaria

Quinine in Pregnancy In cases of malaria with pregnancy it is desirable that drugs other than quinine such as chloroquine camoquine or mepacrine should be used but in case of their non availability quinine should not be withheld for fear of abortion

Difficulties with Quinin Treatment 1 Patients refuse to take quinine for its unpleasant and bitter taste 2 There is a strong objection to taking quinine in adequate doses for the unpleasant symptoms of cinchonism e g headache giddiness ringing in the ears deafness nausea vomiting photophobia 3 Prescribing inadequate doses to avoid cinchonism 4 The frequent occurrence (50 per cent) of relap es even after adequate treatment with quinine 5 Abscess and sepsis following intramuscular injection 6 Shock and collapse following intravenous injection 7 Undesirable signs and symptoms that follow the administration of quinine in very mall doses in ca es with sensitivene s to quinine e g dyspnœa dysphagia rash (urticarial

occasionally hæmorrhagic) itching nausea vomiting diarrhœa blood with stool hæmoglobinuric fever severe prostration palpitation collapse syncope

Toxic Effects of Quinine In daily doses of 15 20 grains for 7 days quinine has no deleterious effect on the general health of the patient But as it is a protoplasmic poison it produces toxic symptoms when taken in large doses or for a prolonged period even in moderate dose

The toxic effects may be

1 *Mild*—such as nausea tinnitus giddiness insomnia tremor and palpitation

2 *Severe*—symptoms due to idiosyncrasy or acquired hyper sensitiveness Such symptoms may occur even with a small dose of quinine ($\frac{3}{4}$ 1½ grains)

(*a*) Rise of temperature

(*b*) Cutaneous symptoms—œdema of the skin (specially of the eyelids) eruptions which may be erythematous scarlatiniform urticarial and hæmorrhagic exfoliative dermatitis

(*c*) Hæmorrhages from mucous membranes—serious hæmo globinuria in susceptible persons even after a single dose

(*d*) Gastro intestinal symptoms—dysphagia vomiting diarrhœa melæna

(*e*) Disturbances of vision and hearing—amaurosis permanent deafness—though rare

(*f*) Respiratory symptoms—dyspnœa acute pulmonary œdema

(*g*) Circulatory symptoms—palpitation collapse syncope

Common Causes of Failure of Quinine Therapy and of Relapses

1 Lack of a high grade of natural immunity and interference with the development of acquired immunity by the use of large doses of quinine over prolonged periods in the primary acute attack

2 Inadequate amount of quinine administered

3 Improper way of administration and use of unsuitable pre parations such as tablets with impervious coating

4 Adulteration of quinine

5 Existence of bad water in the circulatory system such as the spleen and the bone marrow where the drug cannot reach and act on the few residual parasites which may lurk and multiply there

6 Presence of so called quinine resistant parasites—the existence of such parasites is very doubtful

7 Non absorption of quinine when given per mouth due to some associated gastro intestinal disease It is also very doubtful

8 Presence of several species of parasites—doubtful

9 Quinine has no action on pre and exo erythrocytic forms It is therefore not a causal prophylactic and cannot prevent *P. vivax* relapses

TOTAQUINA There are two types of totaquina available Type I and Type II

The chief alkaloids in Type I are quinine and cinchonidine and in Type II cinchonine

Totaquina Type I is a mixture of alkaloids from the bark of *Cinchona succirubra* and other varieties of cinchona plants It is standardised to contain at least 70 per cent of crystallizable cinchona alkaloids of which at least 15 per cent must be quinine In doses of 20 grains of Type I it is almost as effective as quinine in reducing fever and clearing the peripheral blood of malaria parasites in the ordinary cases of malaria It is stated that totaquina is more irritant to the stomach than quinine and because it contains cinchonidine it is liable to produce headache or even convulsions in toxic doses

CINCHONA FEBRIFUGE This term has been loosely used in the past to signify (1) the total alkaloids extracted from cinchona bark and also (2) the residual alkaloids which remain after quinine has been separated from total alkaloids So the composition of cinchona febrifuge is very variable If the total alkaloids be used the efficacy of cinchona febrifuge in daily doses of 15 grains is nearly as high as that of quinine and at the same time it is much cheaper than quinine The substance which is actually sold as cinchona febrifuge in 3 grains tablets usually consists of the residual alkaloids

Advantage It is very cheap and costs half as much as quinine and is therefore suitable for mass treatment

Disadvantages 1 Tendency to produce nausea

2 Its variable and unknown composition

3 It is less effective than quinine in malignant tertian malaria

Dose It may be used in the same dosage as quinine

QUININE DERIVATIVES ARISTOCHIN It is a quinine derivative containing 96 1 per cent quinine The advantage of this drug is that being a tasteless preparation it can be given to children or to those who object to quinine for its bitter taste It is insoluble in water and is generally prescribed in the form of powder

Dose 1 to 10 grains

EUQUININE (Quinine Ethyl Carbonate) It is also a quinine derivative almost tasteless and sparingly soluble in water It may be given to children in the form of powder Its dose should be one-and a half as much as that of quinine sulphate because it is not so well absorbed from the gastrointestinal tract as quinine sulphate

Dose 1½ to 15 grains

SYNTHETIC ANTI MALARIAL DRUGS MEPACRINE (QUINACRINE ATEBRIN) It is a dihydrochloride of an alkylamino acridine derivative produced in 1930 by Schulemann available in the form of a yellow powder and also in the form of tablets each containing 0 1 g of the drug It is bitter to the taste oluble in water (1 in 14) forming a neutral solution Mepacrine is absorbed rapidly from the duodenum and excreted in the bile It also appears in the urine after an hour of its administration The excretion in urine though rapid at first may go on slowly for as long as 5 weeks The drug tends to accumulate in liver gallbladder intestine and upper part of stomach It is also secreted in milk of nursing mother

Mode of Action The antimalarial action is influenced by the concentration of the drug in the plasma Effective plasma concentration is 30 micrograms per litre of blood Mepacrine is effective against the asexual forms of all the four species of malaria and the sexual forms of these species excepting those of the malignant tertian malaria Mepacrine and quinine in ordinary therapeutic doses are equally effective in the treatment of acute attacks of benign tertian and quartan malaria The action of mepacrine is probably direct on the parasites the different forms of parasites being affected like quinine Mepacrine is however considered to be superior to quinine in the treatment of acute attacks of malignant tertian malaria because of its more rapid action on the trophozoites than that of quinine On some strains of *P falciparum* (West African) however quinine is more effective than mepacrine Relapses may occur after treatment with mepacrine but less frequently than after quinine treatment

Advantages 1 Mepacrine can be safely and effectively given to (*i*) patients sensitive to quinine (*ii*) pregnant women and (*iii*) patients suffering from blackwater fever In some cases however mepacrine may not only fail to control blackwater fever but may precipitate it

2 It causes less frequent vomiting and does not give rise to nervous symptoms such as tinnitus and deafness as does quinine

3 The course is shorter than that of quinine (5 7 days)

4 The temperature is more quickly controlled and the blood is cleared up of parasites more rapidly (in 4 5 days) though the splenic enlargement disappears more slowly than with quinine

5 Mepacrine does not cause any albuminuria nor any toxic myocarditis with lowering of bloodpressure

Modes of Administration Oral route Mepacrine tablets of 0 1 g each are given to adults three times a day after meals for 5 7 days For a rapid control of acute malarial symptoms the following scheme is preferable—1st and 2nd days 6 tablets and later on 3 tablets daily The course of mepacrine may be followed after an interval of 3 days by plasmoquine 0 01 g daily after meals for 5 days to destroy the gametocytes and reduce the relapses in *P vivax* and *P malaria* infections There is no advantage in combining quinine and mepacrine in the treatment Mepacrine and plasmoquine should not be administered simultaneously because such a combination is likely to produce toxic symptoms

Dose In children

1 to 2 years	¼ tablet daily
3 to 4 years	½ tablet daily
5 to 8 years	1 tablet daily
9 to 12 years	2 tablets daily
13 years and over	Same as in adults

Intramuscular route Mepacrine methanosulphonate is a soluble compound suitable for intramuscular administration Mepacrine methanosulphonate in doses equivalent to 0 3 g of hydrochloride dissolved in 5 c cm of sterile distilled water is preferably given intramuscularly in malignant tertian cases with pernicious symptoms like coma convulsions hyperpyrexia dysentery and diarrhœa and vomiting It is seldom necessary to repeat the injection within 24 hours Pain at the site of injection may be complained of in about 25 per cent of cases though it is less than that associated with the intramuscular injection of quinine Occasionally deep abscesses may form locally After 1 2 injections mepacrine should be continued orally

Mepacrine has been used intravenously but it is better to avoid it for fear of toxic reactions In severe malaria parenteral quinine is usually preferred to mepacrine unless the former is contraindicated

By effects Serious by effects after the administration of mepacrine are definitely uncommon Headache loss of appetite slight and occasional epigastric pain and vomiting (12 per cent cases) diarrhœa

feeling of extreme prostration slight fall of bloodpressure and hæmoglobinuria may occur after administration of mepacrine due to personal idiosyncrasy Occasionally in less than one in one thou and treated cases mental disturbances such as mania confusion amnesia may occur and last for a few hours to a week Epileptiform convulsions and spasms may also supervene The drug may produce a yellow staining of the skin and mucous membrane usually after the third day in one third of the cases It is due to a harmless deposition of the dye in the skin which clears up in 1 to 4 weeks after cessation of the treatment though in exceptional cases it may persist for 3 months

PROGUANIL OR PALUDRINE. Curd Davey and Rose (1945) synthesised this new antimalarial remedy It is a complex diguanide compound

It has a bitter taste and is slowly soluble in water It has no action on sporozoites It is said to be effective against exo erythrocytic forms of *P falciparum* It acts directly on the asexual forms especially in their schizont stage inhibiting nuclear division and producing degenerative changes in the parasites It cannot prevent the appearance of gametocytes crescents have been known to be present for a long time It is however said to have some devitalising effect on the gametocytes which do not grow beyond the oocyst stage in a mosquito during or shortly after (7 days after average dosage) paludrine therapy It is rapidly absorbed and rapidly excreted effective plasma concentration being approximately 20 to 40 micrograms per litre

It is available as *paludrine* (hydrochloride) in 100 and 300 mg tablets Average dose is 600 mg in 2 or 3 doses for the first 1 or 2 days and thereafter 300 mg a day for 5 days which is usually sufficient to control the acute attack and make peripheral blood parasite free Thereafter a dose of 100 mg twice a week or 300 mg once a week may be continued for 4-6 months Relapse rate in benign tertian malaria without suppressive treatment is very high (about 40 per cent)

Paludrine is relatively slow in action and some strains of *P falciparum* are resistant to it The use of paludrine alone in falciparum malaria is therefore risky Paludrine lactate has been used intravenously and intramuscularly but the latter route is painful Besides in ca es of emergency requiring parenteral therapy quinine is the drug of choice Parenteral paludrine therefore has practicallly no place in the treatment of malaria

Toxicity Paludrine in high doses (usually 0 8 g daily) often causes toxic symptoms *e g* gastrointestinal irritation (nausea vomiting

diarrhœa griping) and occasionally renal irritation (albuminuria hæmaturia)

Advantages Readily available cheap nontoxic in therapeutic dose It is safe in pregnancy

Disadvantages Slow action Some strains of *P falciparum* are resistant to paludrine

CHLOROQUINE is a quinoline derivative having the properties somewhat similar to those of mepacrine but it does not stain the tissues It is however 3 times as active as mepacrine It is highly effective against the asexual forms of all parasites which are cleared off the peripheral circulation within a day or two It has however no action on either the sporozoites or the exo erythrocytic forms Gametocytes especially the crescents are not affected It is more useful in benign tertian than in malignant tertian malaria Early relapses are not common with chloroquine

It is available as a white tablet each containing 0 15 g base In acute malaria a course of 10 tablets in three days (4 tablets immediately 2 tablets after 6 hours on the first day and 2 tablets each day for next 2 days) is sufficient to control the paroxysm within a day or two Two tablets a week is reported to be a successful suppressive dose The drug is well tolerated toxic symptoms like transient headache insomnia visual disturbances pruritus asthenia slight gastrointestinal disturbances occur in not more than 10 per cent of cases

CAMOQUIN is another synthetic drug of quinoline derivative It is much more active but less toxic than mepacrine with little or no yellow staining of the tissues and is equally effective in all the three forms of malaria with results comparable to those of chloroquine It is available in 0 2 g tablets The usual dosage is 0 2 g t d s on the 1st day and 0 2 g once daily for next 2 days It may also be given in a single dose of 0 6 g For suppression of malaria 0 2 g weekly or 0 4 g fortnightly has been found to be effective

PLASMOQUINE This is a complicated synthetic organic compound derived from quinoline It is available as pamaquine naphthoate in the form of tablets of 0 02 gramme each

Advantages 1 It acts on and destroys the sexual parasites of all the four species specially those of *P falciparum* which are not acted upon by quinine or even mepacrine

2 Due to its gametocidal action it is an important drug in controlling the spread of malaria

3 In combination with quinine it reduces the relap e rate in cases of benign tertian and quartan infections This appears to be due to its action on exo-erythrocytic forms of malaria parasite

Inspite of all the e advantages the use of plasmoquine is solely restricted to prevent relap es and spread of malaria It is not used alone for the treatment of acute attacks because the margin of safety between the toxic dose and the effective therapeutic dose is very narrow

Disad antages 1 It has got no destructive action on the asexual parasites of *P falciparum* and has got a slight action on those of *P i ax* and *P malariæ* as compared to that of quinine

2 It frequently produces toxic symptoms The toxic effects of the drug which depend more on individual idiosyncrasy than on large dosage are (i) Epigastric pain anorexia nausea vomiting and diarrhœa (ii) Dizziness (iii) Cyanosis due to methæmoglobinæmia (in 7 per cent of cases) (i) Interference with the new formation of hæmoglobin after prolonged use (v) Jaundice due to toxic hepatitis (in 3 5 per cent of cases) (i) Methæmoglobinuria and transient albuminuria (ii) Coma collapse and even death

Dose Pamaquine naphthoate is given in doses of one tablet of 0 02 g (45 per cent base) three times a day after meals for 7 10 days with or following a schizonticidal drug The drug is to be stopped on appearance of cyanosis or abdominal pain

Combined Quinine and Pamaquine Therapy Cases of relapsing benign tertian or quartan malaria may be treated with a daily dose of 15 to 20 grains of quinine sulphate in mixture with 0 02 g (about 9 mg base) of pamaquine naphthoate twice daily for 10 days

Primaquine is a new member of the 8 amino quinoline group of drugs It is less toxic and appears to be more effective than pamaquine or any other member of the family Like pamaquine it eradicates the gametocytes and is used in combination with a schizonticidal drug for the radical cure of *P i ax* malaria

The drug is used in a dose of 15 mg daily (preferably in single administration) for 10-14 days Quinine (5 7 grains t d s) should al o be given for the first 7 days or chloroquine for the first 3 days (0 6 g for 1st dose 0 3 g 6 hours later and 0 3 g for next two days)

The relapse rate with this regimen is low (less than 10 per cent)

Toxicity In therapeutic dose gastrointestinal irritation and rarely hæmolysis may occur

PENTAQUINE is a 8 aminoquinoline derivative which like plasmoquine is effective against the exo erythrocytic form of parasite It is less toxic than plasmoquine A dose of 60 mg pentaquine base daily used along with quinine reduces relapse in *P vivax* malaria in the same way as pamaquine A related compound *isopentaquine* appears to be even less toxic than pamaquine

PYRIMETHAMINE OR DARAPRIM This new addition to synthetic antimalarials is a pyrimidine derivative and has been found to be very active against *P gallinaceum* in chicks and *P berghei* in mice Its action in human malaria is not very promising A benign tertian or quartan infection subsides in about 2 3 days time but it fails to cure a third of malignant tertian infection For treatment of a clinical attack two doses of 50 mg are given on consecutive days A weekly dose of 25 mg is a fairly effective suppressant for semi immune people

SYMPTOMATIC TREATMENT

It should be emphasised that many of the symptoms disappear on prompt institution of the specific treatment

Intense Headache Aspirin or phenacetin in gr v doses may be given

Mild Vomiting associated with Gastritis Quinine in an effervescing mixture may be given as it is retained more readily

Persistent Nausea or Vomiting In such cases quinine is given intramuscularly or intravenously For the vomiting pieces of crushed ice sips of hot water liquor iodi mitis in minim doses or even a subcutaneous injection of sodium luminal gr iii in 1 c cm of sterile distilled water or gr 1/100 of atropine sulphate with morphine hydrochloride gr ¼ should be given The following powder may be helpful—

R/

Hydrargyri subchloridi	gr ½
Sodii bicarbonatis	gr v

Fiat pulvis

One dose may be given ½ hourly for 4 doses

Adrenaline 10 minims by injection may also be given its beneficial action has been attributed by some authorities to the correction of associated hypo adrenia Intravenous glucose should be given and feeds withheld Chlorpromazine in 10 25 mg dose once or twice daily by mouth gives good results

Hyperpyrexia Ice bag may be applied on head and an attempt should be made to bring down the temperature by cold sponging cold baths ice cradling or iced rectal saline

Circulatory Failure The objects of the treatment of the circulatory failure in the algid cases are to maintain

(*a*) Blood volume

(*b*) Peripheral vascular tone

The blood volume may be replenished and maintained by

(*i*) Intravenous administration of 50-100 c cm of 25 per cent solution of glucose twice daily

(*ii*) Subcutaneous administration of 15 20 ounces of 5 per cent glucose in physiological saline (or in distilled water where there is threatening œdema of lungs)

(*iii*) Plenty of fluids by mouth such as barley water *dab* water lemonade glucose water etc

(*iv*) Rectal administration of 5 per cent glucose in normal saline or distilled water by the drip method

The peripheral vascular tone may be maintained by the

(*i*) Stimulation of the vasomotor centre by the subcutaneous use of *cardiazol* 1 c cm or *coramine* 2 c cm *icoral* 2 c cm caffeine sodium benzoate gr v in 2 c cm

(*ii*) Stimulation of the vasomotor system (peripheral) by subcutaneous administration of ½ c cm of adrenaline 1 in 1000 solution or of pituitrin 1 c cm The action of adrenaline however is transient lasting for about half an hour

(*iii*) Stimulation of the vasomotor system (both central and peripheral) by the hypodermic injection of cardiazol ephedrine 1 c cm or *veritol* 2 c cm

Coma and Convulsions in Cerebral Malaria Intravenous quinine may be usefully supplemented by

(*i*) Elevation of the head end of the bed to reduce cerebral congestion

(*ii*) Rectal administration of 6 to 8 ounces of 25 per cent solution of magnesium sulphate by the drip method 5 c cm of 20 per cent solution may also be given by the intra muscular route

(*iii*) Intravenous administration of 50-100 c cm of 50 per cent sterile glucose or preferably sucrose solution twice daily to reduce the intracranial pressure by the drainage of the ventricles

(*iv*) Lumbar puncture to relieve the raised intracranial tension and the associated cerebral œdema

( ) Intramuscular injection of sodium phenobarbitone gr iii in 1 c cm of distilled water if necessary

ANÆMIA Hypochromic anæmia of varying grades is usually present in acute malaria and specially in chronic cases When the anæmia is marked oral administration of a suitable preparation of iron in adequate doses is necessary In the choice of an iron preparation it should be remembered that its activity when taken by mouth depends on its solubility and its yield of free ferrous ions

Any of the following preparations may be tried daily in divided doses and one hour after meals for a month —

Dessicated ferrous chloride	gr 9
Ferrous sulphate	gr 18
Ferri et ammonii citratis	gr 90
Freshly prepared Blaud s pill (Pilula ferri carbonatis)	gr 60

or any effective proprietary preparations of iron available in the market

CLIMATIC TREATMENT

If the patient suffers from repeated attacks of malaria he may be sent for a change to a healthy and malaria free place where he should however continue the anti malarial treatment for a few weeks

TREATMENT OF RELAPSE

Relapse should be differentiated from *recrudescence* which means a return of clinical symptoms within a short time after the primary attack whereas *relapse* occurs after an interval of weeks or months during which the patient enjoys a good health and is free from any clinical symptoms of malaria

The antimalarial remedies may not eradicate all the parasites from the human host during the treatment of a primary attack Some of them survive and continue the schizogony cycle till under conditions of lowered resistance uch as chill fatigu exposure to heat the febrile threshold is reached and relapse occurs within 2 8 weeks of the primary attack

This schizogony is however kept well below the febrile threshold by several factors

1 The natural powers of resistance of the infected person exert their influence under which some of the parasites are phagocytosed by the large mononuclear cells carried to the spleen liver and bone marrow and disintegrated there by the reticulo endothelial cells Others are converted into gametocytes which do not take up the schizogony cycle

2 The development of an acquired immunity (*premunition*) The merozoites that are killed either by antimalarial remedies or by the powers of natural resistance act as an antigen and stimulate the formation of an immune body which as it reaches a high level eradicates the infection The immune body is usually specific against the strain of the infecting parasite and does not protect against infection by another strain of the same species But repeated infections with immunologically different strains which are particularly numerous in *P vivax* infection may in time give rise to a true general immunity to all the malarial strains of the locality The immunity that develops as the result of the continuance of a low grade malarial infection is called *premunition* and the process of acquiring it is impeded by prolonged treatment with large daily doses of quinine or any other antimalarial drug at the first onset of fever in the primary attack and in each relapse The liability to relapse varies with the species of the malaria parasite It is most common and persistent in quartan infection which may relapse up to 19 years Relapses in benign tertian infection may occur up to 4 years In malignant tertian malaria relapses are less frequent and do not occur after 1 year

The control and prevention of relapses may therefore be achieved by (1) raising the defensive power which the infected person possesses naturally or acquires as the result of previous attacks and (2) administration of suitable and effective antimalarial drugs in adequate dosage

The comparative value of the different antimalarial remedies in the control of relapses in vivax malaria may be seen from the following table —

Antimalarial drug	Percentage of relapse
Quinine	over 50
Quinine + plasmoquine	10
Quinine (or chloroquine) + primaquine	below 10
Mepacrine	over 34
Paludrine	40
Paludrine + plasmoquine	13

TREATMENT OF CHRONIC MALARIA

The treatment of a chronic malaria infection is based on the following principles —

1 Improvement of the general health by an adequate balanced diet rich in protein and vitamins Appropriate measures are adopted to treat associated conditions such as anæmia of hookworm infection amœbiasis

2 Control of the febrile attacks by the use of quinine dihydrochloride gr xv a day till the temperature subsides After this small doses of quinine for long periods cause a marked reduction of the splenic enlargement

3 Increase of non specific immunity by intramuscular injections of non specific protein substances such as milk peptone and T A B vaccines

4 Increase of the specific immunity by promoting the periodic outpouring of the malaria parasites into the blood stream and exposing them to the phagocytic activity of the reticuloendothelial cells This object is achieved by the intravenous injections of adrenaline in gradually increasing doses from 1/100 mg to 1/10 mg until 30 injections are given—the last dose being repeated for 20 days The results of this treatment are satisfactory because the febrile attacks are cut short spleen is markedly reduced in size the general health and blood picture improve considerably the parasiticidal action of anti malarial remedies subsequently used is accelerated The immediate reactions following the intravenous use of adrenaline such as pallor headache retrosternal pain tachycardia tremors and arrhythmia are transitory and not dangerous

PREVENTIVE MEASURES

The prevention of malaria may be considered under the following two headings —

(a) Individual prophylaxis by drugs

(b) Community prophylaxis by drugs and hygienic measures

INDIVIDUAL PROPHYLAXIS OR CHEMO PROPHYLAXIS *Quinine and its Allies* Quinine and the cinchona alkaloids do not act as prophylactics in the true sense of the term They have no action on the sporozoites or exo erythrocytic forms and so cannot prevent infection But it is a fact that mass administration of quinine (which is of course very expensive) or of totaquina causes definite reduction in the incidence of malaria But the following drugs are more effective than quinine for clinical prophylaxis

Mepacrine This drug which is also not a true causal prophylactic is used as a clinical prophylactic in doses of 0 2 g a day twice a week with two clear days interval between each dose or better 0 1 g daily for 6 days in a week for months and it does not lead to any marked colouration of the skin and its prophylactic value is superior

to that of quinine It should be taken for at least three weeks before entering and after leaving a malarial place in the dose of 0 1 g daily The first three weeks course may however be replaced by a loading dose to start with to bring up the effective blood concentration

Doses for children—

Upto 2 years	0 05 g biweekly
3—4 years	0 1 g
5—8 years	0 15 g
9 years and over	0 2 g

Paludrine in dose of 0 1 g every two to three days acts practically as a causal prophylactic in malignant tertian malaria Benign tertian malaria is however only suppressed with this dose Alternatively 0 3 g may be taken once a week

Chloroquine 0 3 g or *camoquin* 0 2 g once a week is a very effective prophylatic (suppressive) drug Camoquin 0 4 g fortnightly has also similar action

Plasmoquine Plasmoquine has got a gametocidal action on all the four species of malaria parasites hence it is an effective drug in the prevention of the spread of the infection So following the usual course of quinine or mepacrine treatment it is used in doses of 0 01 g twice a day after meals for 5 days Primaquine may be used instead

Daraprim 25 mg weekly is reported to suppress malaria

COMMUNITY PROPHYLAXIS Malaria will be eradicated if any of the following conditions is fulfilled —

1 Eradication of the malaria parasites from the infected persons by a thorough treatment and maintenance of a high grade immunity

2 Protection of the community against the bites of the carriers This is achieved by providing mosquito nets and mosquito proof clothing Mosquitoes should also be prevented from biting infected persons a malaria patient should always use a mosquito net for protecting the community Repellents like dimethyl phthalate may be used to keep away the vectors

3 Extermination of the vectors Larval breeding can be controlled by avoiding construction of man made breeding places and eliminating unnecessary collections of stagnant water The larvae may be killed by larvicides like pyrethrum and D D T Imagos and adult mosquitoes are best killed by insecticides like pyrethrum or D D T used as sprays

Eradication of Malaria Parasites from the Infected Persons To eradicate the malaria parasites from the blood of infected persons in a locality it is necessary to measure the amount of malaria in that locality Extent of malaria may be measured best by splenic index and parasitic index of children between the ages of two to ten years born and brought up in that locality The splenic index and the parasitic index of adults of that community are of little value because they are more or less immune to the local strains of malaria The splenic index of the children gives the measure of endemicity and the average splenic enlargement that of intensity in that locality

The following classification is generally adopted during malaria survey in India

Spleen rate more than 50 per cent —Hyper endemic
Spleen rate 25 to 50 per cent —Highly endemic
Spleen rate 10 to 25 per cent —Moderately endemic
Spleen rate less than 10 per cent —Healthy

So in localities where the child spleen rate is more than 10 per cent all the children up to the age of ten if not all the inhabitants with enlarged spleen or malaria parasites in their blood or both should be treated thoroughly with quinine and plasmoquine for 5 days to prevent infection of the carrier mosquitoes with malaria parasites and thereby to prevent the spread of infection to the human hosts

BLACKWATER FEVER

[Hæmoglobinuric Fever Malarial Hæmoglobinuria.]

DEFINITION

It is an acute disease characterised by high fever of sudden onset associated with rigor vomiting jaundice scantiness or suppression of urine and hæmoglobinuria This condition is one of the manifestations of malignant tertian malaria in which there is an extreme intravascular hæmolysis resulting in hæmoglobinæmia and consequent hæmoglobinuria.

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It occurs in places where malaria is endemic and very severe and where malaria of the malignant tertian type is very prevalent Its chief home is Tropical Africa In Europe it is found in Bulgaria Macedonia Albania Greece Sicily and Sardinia In America it is found in the southern states of the Union and also in Central America In Asia it is present in Palestine Malay Peninsula Formosa Burma Northern Siam and in Yunnan of China In India it is common in Terai Dooars Jalpaiguri Burdwan Hooghly and other districts of West Bengal Singbhum district of Bihar and in Meerut and Amritsar

SEASONAL PREVALENCE It occurs usually during and immediately after the rainy season At times it appears to assume an epidemic form but generally it occurs sporadically

AGE AND SEX INCIDENCE Individuals of all ages are liable to blackwater fever but it is most commonly seen in adults and middle aged people perhaps due to their greater exposure to causative factors Both sexes are equally liable but the disease is more frequently seen in men on account of their greater exposure to circumstances conducive to an attack

RACE. Europeans and the Chinese are the chief victims but it is also commonly seen amongst the Egyptians in Sudan

PREDISPOSING CAUSES 1 Residence in an area of intense endemic malaria for a period of six months to four years

2 Repeated attacks of malignant tertian malaria with imperfect quinine treatment A single infection however severe is rarely the cause of blackwater fever

3 Debility from previous illnesses
4 Alcoholism

EXCITING CAUSES 1 Quinine even in small doses
2 Exposure to cold or extreme heat
3 Fatigue
4 Alcohol in excess
5 Administration of plasmoquine and occasionally even mepacrine in some cases and less frequently use of the drugs like methylene blue phenacetin antipyrin and salvarsan

THEORIES OF CAUSATION The exact causative factor of blackwater fever is not yet definitely known The following theories have been put forward as to its causation

Malaria Theory 1 Most prominent workers agree that the condition is nothing but a manifestation of hypervirulent type of malignant tertian malaria and according to their opinion Malarial hæmoglobinuria would be a more appropriate term for the condition

Points supporting the theory (*a*) It occurs in places infested with malignant tertian parasite

(*b*) It occurs in people who have suffered from repeated attacks of malignant tertian malaria

(*c*) It occurs in the malaria season

(*d*) Malaria parasites and increase of monocytes have been found in the blood in 95 6 per cent of cases just before the onset of hæmoglobinuria The parasite almost invariably found is *Plasmodium falciparum* though the benign tertian and quartan parasites have also been occasionally found There may be mixed infections

(*e*) Clinical signs and symptoms of blackwater fever closely simulate those of malignant tertian malaria

(*f*) Prevention of malignant tertian malaria abolishes blackwater fever

(*g*) Blackwater fever has been observed in cases of general paralysis of the insane after an artificial inoculation with certain strains of *Plasmodium falciparum* for therapeutic purpose

(*h*) Hæmoglobinuria has been produced in monkeys (*Macaca rhesus*) heavily infected with *Plasmodium knowlesi*

Points against the theory (*a*) Blackwater fever does not invariably occur in places where malaria is endemic

(*b*) Many people suffer from malaria but only a small number of them get hæmoglobinuria

(*c*) It has occurred in apparently healthy persons who seem to have never suffered from malaria during their residence in endemic areas

(*d*) Malaria parasites have seldom been found during an attack of blackwater fever

(*e*) No definite incubation period can be detected at the onset of hæmoglobinuria

From a consideration of the above points it appears that blackwater fever is not directly due to the action of any special malaria parasite but is to be considered as a reaction of the body to a prolonged and recurrent infection with *Plasmodium falciparum*

The view that blackwater fever is caused by a special hæmolytic strain of *P falciparum* has not been confirmed by the production of hæmoglobinuria in any of the mental patients inoculated with the blood of blackwater fever patients drawn at various times after the occurrence of hæmoglobinuria (*Foy and Kondi*)

2 *Quinine Theory* The idea that quinine might produce blackwater fever originated from the fact that in most cases a history of taking quinine about two to three hours before the onset of hæmoglobinuria is almost always available and so it is naturally inferred that quinine is the causative and precipitating factor It has recently been suggested that quinine renders the red cells of malaria patients more sensitive to the action of intravascular lysis But a consideration of the following facts shows that quinine cannot be the primary factor in the causation of blackwater fever

Points against the theory (a) All quinine takers do not get blackwater fever

(*b*) Quinine even in toxic doses has never produced hæmoglobinuria in healthy people unless susceptible to quinine or in persons not suffering from malignant tertian malaria

(*c*) Quinine when given to malaria patients in adequate doses and in a regular manner will never produce hæmoglobinuria

(*d*) Blackwater fever has been reported in persons who have never taken quinine but had taken plasmoquine mepacrine or proguanil

(*e*) Blackwater fever was known to Hippocrates long before the introduction of cinchona in the treatment of malaria

3 *Modern Theory* The most modern and the usually accepted view is that blackwater fever is essentially a hæmoglobinuric fever

Malaria alone or quinine alone is rarely capable of causing this disease Three factors appear to co operate together to produce the condition

(*a*) Formation of an intracellular hæmolysin in excess of normal due to the activity of hypertrophied reticuloendothelial system resulting from repeated attacks of *P falciparum*

(*b*) Presence of an exciting factor such as the administration of quinine or plasmoquine exposure to cold or over exertion which causes a sudden contraction of the spleen and liberation of this hæmolysin into the circulation the latter being immediately fixed to the red cells

(*c*) Susceptibility of the individual A low cholesterol content of the blood often present in chronic malignant tertian malaria predisposes to the attack by increasing the vulnerability of the red cells to the action of the hæmolysin A chronic deficiency of vitamin C in the diet may also play some part in diminishing the amount of anti hæmolysin

In support of the probable existence of a special hæmolytic predisposition of the infected individuals the points are

1 Occurrence of blackwater fever in some cases of general paralysis of the insane artificially inoculated with certain strains of *P falciparum* 2 Occurrence of hæmoglobinuria in certain species of monkey (*Macacus rhesus*) infected with *P knowlesi* and not promptly treated

Other theories recently advanced regarding the pathogenesis of blackwater fever can be briefly stated as follows

1 Upset of the normal balance between the lytic tissue factors and their natural inhibitors due to changes in plasma agglutinin pattern brought on by plasmodination of erythrocytes The hæmolysis of blackwater fever is probably due to a reduction in the amount of the inhibitory factor in the presence of a normal concentration of the lytic agent (Maegraith Findlay and Marten 1943 Maegraith 1946)

2 Gear (1946) has suggested that the invaded red cell behaves as an autoantigen and produces antibody which acts as an autolysin in the presence of complement causing hæmolysis

PATHOLOGY

There is no certain knowledge of the exact mechanism of hæmolysis in blackwater fever There is however an extensive intra vascular destruction of red blood corpuscles specially in the venous sinuses of the spleen with rapid liberation of an excessive amount of

oxyhæmoglobin in the blood stream which the reticuloendothelial system is not able to deal with in the normal manner

Most of the free oxyhæmoglobin is converted into methæmalbumin (pseudo-methæmoglobin)—a derivative of hæmoglobin closely allied to methæmoglobin It is not excreted in the urine because the molecules are too large to pass through the glomerular filter

A large part of the oxyhæmoglobin is disposed of by formation of bilirubin leading to hyper bilirubinæmia and polycholia which give rise to jaundice of the hæmolytic type bilious vomiting bilious diarrhœa and urobilinuria

A small portion of it (not more than 36 per cent of the liberated oxyhæmoglobin) is excreted in the urine as such If the pH of urine is below 6 0 some of it is converted during excretion into acid hæmatin which is insoluble and blocks the renal tubules

Lastly a considerable portion is however converted into methæmoglobin *not in the plasma but in the renal tubules during excretion* in the urine to which it imparts the characteristic black colour

MORBID ANATOMY

The histo pathology of blackwater fever is almost the same as that of malignant tertian malaria

BLOOD As a result of the excessive intravascular hæmolysis severe anæmia at the onset is a prominent feature but on the 3rd or 4th day of convalescence polychromasia and reticulocytosis are often seen Malaria parasites may be found in the blood in the beginning of fever but they disappear rapidly during the process of hæmolysis They may reappear during convalescence some days after the attack A moderate leucopenia with increase of large mononuclear cells and pigmentation of the leucocytes is a common finding

SPLEEN It is soft slightly or moderately enlarged dark red in colour due to congestion and pigmented with hæmozoin Histological examination shows the splenic pulp filled with large mononuclear cells and endothelial cells containing red cells and hæmozoin pigment (hæmatophagy) The endothelial cells lining the sinuses contain al o the iron containing pigment—hæmosiderin Malaria parasites are usually scanty or not found at all

LIVER. It is of olive brown colour Enlargement is slight or moderate Congestion and pigmentation are both present The hepatic parenchyma shows areas of atrophy and fatty change The liver cells

usually contain a large amount of the yellow pigment—hæmosiderin The hepatic capillaries are distended and the Kupffer s cells are often loaded with hæmozoin pigment

GALL BLADDER It is found to be distended with thick dark green viscid bile

KIDNEYS They are enlarged congested and have a peculiar greyish violet or brown colour The cortex is swollen The pyramids are also swollen and show dark red striations The tubules are blocked with a brown pigment (acid hæmatin) hyaline and cellular casts Hæmozoin pigment is seen in abundance in the endothelial cells of the capillaries and hæmosiderin in the cells of collecting tubules

In case of death from uræmia the kidneys show evidences of parenchymatous degeneration

BONE MARROW The marrow is brown and of fluid consistency and shows evidences of hyperplasia

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is not definitely known as yet The period of residence in endemic areas of malaria varies considerably in different individuals Blackwater fever occurs rarely during the first six months of residence though a minimum period of fifty days is on record The incidence increases during the next six months and reaches its peak during the second and third years It becomes rare again after five years residence

PRODROMAL STAGE Usually there are no prodromal symptoms of blackwater fever because the onset in most cases is sudden Some authorities suggest the name *pre blackwater state* for some of the clinical manifestations which may precede the onset of the disease It is characterised by a history of repeated attacks of slight fever in a patient infected with the malignant tertian parasite pallor icteric tinge of the conjunctivæ furred tongue moderately enlarged and tender liver and spleen persistent headache constipation high coloured urine containing urobilin and traces of albumin and the presence of a few malignant tertian rings in the blood But this pre blackwater state is not very helpful in deciding which cases will pass on to actual blackwater fever stage

MODE OF ONSET It is usually sudden associated with chill and rigor high remittent fever nausea bilious vomiting aching pain over

the regions of the kidneys urinary bladder liver and spleen and passage of port wine coloured urine

GENERAL APPEARANCE The patient looks very ill and toxic Fallor and anæmia are marked and both occur very rapidly

FEVER It is usually remittent and high (Fig 13) terminating by lysis in a week or so after the hæmoglobinuria has stopped

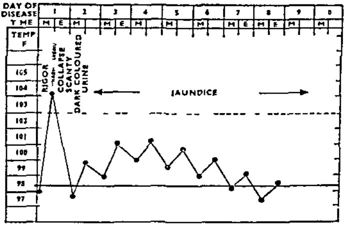


FIG 13 Temperature chart of blackwater fever

Fever may however be intermittent and quotidian associated with rigor during its rise and profuse sweating during the fall In some cases hæmoglobinuria recurs with each rise of temperature Hyper pyrexia may occasionally occur due to the sudden liberation of a large amount of free oxyhæmoglobin into the blood stream

JAUNDICE It appears early It may be slight moderate or very severe In a severe case the jaundice increases with the progress of the fever and the recurrence of the hæmoglobinuric attack and begins to disappear from the fifth or sixth day of return of the temperature to normal

ALIMENTARY SYSTEM The tongue is dry and coated Epigastric pain or distress nausea and bilious vomiting start from the very beginning and persist till the fourth or fifth day Thirst is present Hiccough if present is a serious complication There may be consti pation or bilious diarrhœa according to the severity of the case Spleen is usually *moderately enlarged firm and tender* *Liver is slightly* enlarged and tender

CIRCULATORY SYSTEM The pulse is often very rapid regular weak and of low tension The heart may show varying degrees of enlargement associated with hæmic murmurs and signs of failure due to toxæmia and anæmia

BLOOD Anæmia is marked at the onset The red cells may be as low as 2 millions per c mm with a hæmoglobin of 20 per cent Polychromasia and a reticulocytosis of 5 to 10 per cent occur during convalescence The total leucocyte count is as a rule moderately diminished though the large mononuclear cells are relatively increased and often pigmented Malaria parasites are rarely found in the peripheral blood after the onset of hæmoglobinuria though they are present in most cases just before the onset

There are certain important biochemical changes in the blood of blackwater fever patients such as (1) Increase of methæmalbumin which may be detected spectroscopically (2) Increase of bilirubin which gives a direct delayed van den Bergh reaction The bilirubin index may vary from 5-40 units (3) Reduction of the alkali reserve specially in cases where urine is scanty (4) Moderate increase of urea and non protein nitrogen during the attack and a rise during convalescence—though not invariable (6) Slight increase of oxyhæmoglobin (7) Decrease of serum calcium and diminished coagulability (8) Slight increase of inorganic phosphorus (9) Slight decrease of blood glucose and marked decrease of blood cholesterol

NERVOUS SYSTEM Headache restlessness delirium anxiety a sense of apprehension and a feeling of prostration are often present Convulsion and coma may be present in severe cases

URINARY SYSTEM At the onset the patient complains of aching pain in the loins and over the bladder and passes port wine coloured urine Gradually the lumbar pain increases and the urine gets scantier and darker till it is black After the fifth or sixth day the quantity of urine begins to increase and flow freely and the colour changes from dark to red and gradually to normal appearance again Pain in the loins also gradually disappears In a severe case total suppression of urine may occur on the third or fourth day The present day view of renal failure is that of Maegraith based on the work of Trueta *et al* Renal failure appears to be an example of the syndrome of renal anoxia The anuria is caused by a redistribution of renal blood flow resulting in relative cortical ischæmia with associated changes in the cortical portion of the renal tubules The changes in the renal tubules are similar to what Lucke described as lower nephron nephrosis

If the urine of a blackwater fever patient is made to stand in a tall conical urine glass it separates into two layers the upper one of dark coloured fluid the lower one of brown granular debris forming half to one third of the total bulk. The *reaction of the urine is acid specific gravity is moderately* high Albumin is present in large quantities and it persists for some days even after the hæmoglobinuria has stopped The chemical reaction for hæmoglobin and urobilin is markedly positive The microscopic examination of the urinary sediment shows plenty of brown granular hæmoglobin tube casts hyaline casts a large amount of brown granular debris epithelial cells and a few leucocytes Red cells are often absent Spectroscopic examination shows the characteristic absorption bands of oxyhæmoglobin in the yellow and green between D and E and of methæmoglobin several of which are present in the red between C and D

COMPLICATIONS

In favourable cases on the fourth fifth or sixth day vomiting ceases patient breaks into a profuse sweat temperature gradually subsides urine begins to get clearer and flow freely pain diminishes jaundice begins to disappear and the patient feels better and comfortable and steady convalescence begins If the case be not properly treated during and after the attack the whole picture may repeat itself after a week or ten days *i e* a relapse of blackwater fever may occur

In unfavourable cases the patient gets worse toxæmia deepens and the following complications may appear and be responsible for a fatal termination

(1) Recurrence of hæmoglobinuria on the fourth or fifth day

(2) Continued pyrexia and a typhoid state or occasionally hyperpyrexia associated with cerebral symptoms such as marked delirium convulsions and coma

(3) Acute circulatory failure—(*a*) Peripheral failure due to sudden excessive hæmolysis (*b*) Syncopal failure occurring suddenly even during slight physical exertion or under the strain of repeated and violent vomiting as the result of a toxic myocarditis

(4) Persistent vomiting and hiccough

(5) Suppression of urine and uræmia

(6) Hæmorrhages in the stomach intestines and rarely retina

(7) Secondary infections causing streptococcal septicæmia pneumonia *Esch coli* infection of the urinary tract

(8) Abortion in pregnant women

SEQUELÆ

1 Relapses A blackwater fever patient may have a varying number of relapses even as many as sixteen (*Stephens*)

2 Severe microcytic hypochromic anæmia

3 Cholelithiasis—due to the formation of pigment stones

PROGNOSIS

It depends on the severity of the attack and also on the treatment adopted Suppression of urine hyperpyrexia intense jaundice hiccough uræmia and recurrences of the attack indicate bad prognosis Patients who have had two attacks previously often succumb to the third attack Mortality varies greatly in different epidemics in the same and in different places and under the same treatment Average mortality may be about 25 to 30 per cent

DIAGNOSIS

In most cases the patient himself makes the diagnosis as in places where the disease occurs everybody knows its features well The history of living in a highly malarious area sudden fever with rigor and vomiting passage of blood red urine and appearance of jaundice are all very suggestive of the correct diagnosis

DIFFERENTIAL DIAGNOSIS

1 BILIOUS REMITTENT MALARIA In this disease urine on examination will be found to contain bile and not oxyhæmoglobin Oxyhæmoglobin bands as seen by the spectroscopic examination are absent A simple test to differentiate between oxyhæmoglobin and bile is to dip a piece of white blotting paper for 2 or 3 minutes in the urine If the dark black colour of the urine be due to hæmoglobin the paper will become red but if it is due to bile the paper will become yellow or greenish yellow On examination of the blood numerous malaria parasites will be found in bilious remittent malaria and they persist during the fever till the administration of quinine or mepacrine after which they readily disappear

2 PAROXYSMAL HÆMOGLOBINURIA (*a*) It is a rare condition (*b*) Fever and rigor are much less marked (*c*) Presence of the characteristic black vomit in severe cases (*d*) History of previous attacks under conditions such as exposure to local cold in which occurrence of blackwater fever can be excluded

3 QUININE HÆMOGLOBINURIA It is such a rare condition that

it need hardly be considered It occurs in persons with an idiosyncrasy to quinine History of sensitiveness to quinine history of previous occurrence with quinine in health and other signs of idiosyncrasy are present

4 YELLOW FEVER (*a*) Initial rigor is very slight (*b*) Jaundice and dark urine appear rather late in the disease (*c*) Presence of the characteristic black vomit in severe cases (*d*) Hæmorrhages into the skin and from the mucous membranes (*e*) A falling pulse rate with a steady temperature or a steady pulse rate with a rising temperature (*Faget's sign*) (*f*) Spleen and liver are not usually enlarged (*g*) Hæmoglobinuria is very rare but hæmaturia not uncommon

5 WEIL'S DISEASE (Infectious jaundice) (*a*) Onset with extreme prostration and severe pains in the muscles and joints (*b*) Fall of the temperature to normal with the appearance of jaundice on the 3rd to the 5th day in mild cases (*c*) Presence of petechiæ or hæmorrhages from the mucous membranes on the 3rd to the 5th day in some cases (*d*) Salmon pink conjunctivæ (*e*) Slight or no enlargement of the spleen (*f*) Moderate leucocytosis (*g*) Absence of hæmoglobinuria (*h*) Abundant red cells in urine (*i*) Guinea pig inoculation tests with blood and urine of the patient are positive (*j*) Positive agglutination tests

6 HÆMATURIA It is differentiated at once by detection of the numerous red cells in the urine and by the absence of other special signs and symptoms of blackwater fever

TREATMENT

PRINCIPLES The aim of treatment should be—

(1) to prevent further hæmolysis if possible

(2) to tide over the period of shock

(3) to maintain an efficient circulation and adequate urinary flow and

(4) to relieve the distressing symptoms

GENERAL MANAGEMENT

The patient should be immediately and strictly confined to bed and he must use bed pan and urinal When hæmoglobinuria has started the patient should not be sent on a journey to hospital He should not be allowed to sit even on bed to avoid syncope Patient should be kept warm Skilled and most careful nursing must be arranged for

CARE OF THE BOWELS Strong purgatives should not be used and in the beginning a simple soap and water enema should be given if required Magnesium sulphate may be used later on to move the bowels and also to help biliary drainage

HYDROTHERAPY Patient should be most gently carefully and regularly sponged once or twice daily

Sufficient alkalising fluid must be given to the patient during the height of paroxysm If sufficient fluid cannot be given by mouth or if it is not retained it should be given per rectum or under the skin or occasionally even intravenously About a pint of sterile normal saline given subcutaneously either once or twice a day if necessary is strongly recommended The fluid is gradually absorbed and it dilutes and flushes out the toxin and washes out the hæmoglobin infarcts which plug the renal tubules and thus helps to prevent the suppression of urine

DIET All foods should be withheld during the height of the paroxysm Plenty of alkaline drink glucose water *dab* (green cocoanut) water should be given If nothing can be retained in the stomach due to persistent vomiting 5 per cent glucose in normal saline should be given subcutaneously or per rectum by drip method When vomiting has ceased nourishing liquid diet *e g* fresh milk citrated or diluted with barley water if necessary should be given The patient should be kept purely on milk diet as long as urine contains albumin When steady convalescence has set in and appetite has returned the diet should be more generous and should contain adequate amounts of protein and vitamins

SPECIFIC TREATMENT

There is no drug which is supposed to have any specific action on the disease Moreover at this stage there is no question of specific treatment Specific remedies if there be any should be used to prevent further hæmolysis and hæmoglobinuria and should be used prophylactically to prevent the initial attack *i e* in the pre blackwater state

ANTIMALARIAL DRUGS The most important question is whether to give antimalarial drugs or not There is a difference of opinion regarding the question of administration of such drugs As the disease is considered to be a form of malaria it would seem rational to give such a drug but practical experience teaches one to withhold it during the acute stage

In the stage of blackwater fever the malaria parasites disappear from the peripheral blood hence the antimalarial drugs cannot possibly exert any action on them and so they should be withheld But in those uncommon cases where the parasites persist in the blood the question of giving such drugs will have to be considered very seriously In such cases mepacrine may be given in 0 1 g doses three times daily for 7 days As quinine is considered to be one of the exciting causes of hæmoglobinuria and as its administration is likely to aggravate the condition it is no longer used in the treatment of blackwater fever since the introduction of mepacrine

In those cases in which the parasites have not been found during the acute stage the blood should be carefully examined daily after the acute stage is over for reappearance of the parasites which usually appear in 5 to 14 days after the subsidence of hæmoglobinuria As soon as the parasites are found a full course of mepacrine is given for 7 days

In absence of facilities for examination of blood for the detection of parasites a course of mepacrine for 7 days should be given as a routine in all cases and for 7 to 10 days after the subsidence of hæmoglobinuria to prevent a recurrence of the paroxysm Mepacrine may be replaced by paludrine or chloroquine

VITEX PEDUNCULARIS It has been claimed by many workers to be a specific but there is no convincing evidence as yet of such specificity of this drug It is supposed to promote diuresis and help the elimination of the circulating oxyhæmoglobin in the urine without producing any renal blockade but it has no action once suppression has set in

Freshly prepared infusion of fresh or dried (dried in shade) leaves is used It is given as soon as the diagnosis is made in doses of one ounce every hour or every 2 hours till the appearance of the urine is normal The infusion is then continued in doses of one ounce 4 times daily for a further period of three days The infusion is made by boiling 1 oz by weight of green leaves in 20 oz of water or 1 oz by weight of dry leaves in 40 oz of water for 5 to 10 minutes and allowing them to soak in that water for an hour and strained All loss by evaporation during boiling is made up by adding boiled and cooled water The resulting infusion will have the colour and taste like that of strong tea It is then sweetened with sugar

Tincture vitex peduncularis in doses of m x three times daily may be used during the period of hæmoglobinuria and it may be continued

for 3 to 4 days after the urine is clear It is also available in the form of ampoules of 3 c cm for intramuscular injection The injection may be given once or twice a day according to the severity of the case in addition to the oral administration of the tincture till the ces ation of hæmoglobinuria after which the tincture alone may be continued for a further period of 3 4 days

SYMPTOMATIC TREATMENT

FEVER AND HYPERPYREXIA Hydrotherapy and a simple alkalis ing diuretic and diaphoretic mixture if the patient can retain it Antipyretic such as aspirin antipyrin phenacetin etc mu t be avoided

TOXEMIA AND RESTLESSNES Hydrotherapy—both external and internal sedatives such as sodium luminal bromides or even morphine (1/6 gr) in absence of renal in ufficiency and a mild diuretic and diaphoretic mixture to help the elimination of toxins

VOMITING AND HICCOUGH Calomel in fractional doses and application of hot fomentation or mustard plaster over the epigastrium have been recommended

10 minims of adrenaline solution (1 in 1000) with water may be given orally Pieces of ice by mouth or sips of very hot water may also be tried

✓SUPPRESSION OF URINE WITH COLLAPSE 1 Alkali *e g* sodium citrate and sodium bicarbonate in moderate doses are helpful but not more than 20 g of sodium bicarbonate or its equivalent should be given in 24 hours It has been found that suppression of urine is much less likely to occur when the urine is alkaline Maegraith however ha pointed out that alkalis when pushed in heavy doses may lead to alkalo is

2 Hot fomentations over the loins and application of anti phlogistin or linseed poultice

3 High hot enemata at 100 F

4 No diuretic with the idea of stimulating the kidneys should be given

5 Continuous rectal administration of normal or alkaline aline by drip method

6 Subcutaneous injection of sterile normal saline two or three pints may be given in 24 hours

7 Intravenous injection of alkaline saline containing gr 150 of sodium bicarbonate in a pint of sterile normal saline Thi houl l

be given with caution and not more than one pint at a time so as not to embarrass the left ventricle and produce pulmonary œdema

8 Intravenous injection of 50 100 c cm of 25 per cent glucose solution in distilled water

9 Blood transfusion from a suitable donor or freshly collected stored blood is very helpful in combating renal failure by increasing glomerular filtration pressure and decreasing renal anoxia Serum or plasma is also useful and has the added advantage of much lesser chances of undesirable reactions

ANURIA If anuria persits even after the improvement of the collapsed state adoption of modified Bulls regime is indicated The patient should have in 24 hours 200 g of glucose dissolved in 750 c cm of distilled water either by mouth or intragastric drip in presence of nausea vomiting diarrhœa or flatulence and it is to be continued till the return of renal function With the onset of diuresis care should be taken to replace the lost sodium and potassium

ANÆMIA 1 Adequate doses of suitable iron preparations by mouth 2 Blood transfusion—300-400 c cm of citrated blood from suitable donors in cases of severe anæmia and asthenia

PREVENTIVE MEASURES

The preventive measures are the same as those in malaria All predisposing causes and specially irregular dosing with quinine must be carefully avoided An attack of blackwater fever does not give the individual any immunity but instead makes him more susceptible Patients who are in the pre blackwater state or who had this disease before on the slightest indication of fever should go to bed at once keep himself warm protect himself from draughts and take plenty of warm fluids The patient should keep away from the affected area for the rest of his life if possible In the affected area the subjects of malarial infection should take paludrine chloroquine or camoquin in weekly doses

J C B

CHAPTER IV

LEISHMANIASIS

KALA AZAR

[Visceral le hmania i Bur lwan fever Dum Dum fever Pono]

DEFINITION

Kala azar is a specific disease due to infection with the protozoan parasite *Leishmania dono ani* and is characterised by irregular fever of long duration progressive emaciation anemia enlargement of the spleen and the liver and presence of the causative organism in the cells of the reticulo endothelial system in the spleen liver bone marrow and elsewhere in the ti sues

HISTORY

The disease has existed in Bengal for over one hundred year It was introduced into Assam from North Bengal during the last 30 years of the nineteenth century The parasite was discovered independently by Leishman and Donovan in 1903 and was later named *Leishmania dono ani* The disease *Ponos* prevalent in Greece for over 100 years came to be recognised as kala azar after the discovery of the parasite in 1903 That the disease was prevalent elsewhere was discovered subsequently *e g* in the Sudan in 1903 in Tunis in 1904 in China in 1911 in South America in 1913 In 1904 Chatterjee and Rogers cultivated *Leishmania dono ani* in artificial medium and discovered the flagellate stage The insect vector of kala azar i the and fly was incriminated by Knowles Napier and Smith in 1924 and kala azar was transmitted by the bite of and flies previou ly fed on case of kala azar to su ceptible animals by Smith and co workers in 1940 and subsequently to human volunteers by Swaminath Shortt and Anderson in 1941

Vianna and Marchado introduced in 1913 intravenous injections of tartar emetic in the treatment of South American mucocutaneous lei hmaniasis In 1915 tartar emetic was used by Caronia and Di Cri tina in the treatment of Mediterranean kala azar and by Rogers and Muir in the treatment of kala azar in India The earlier penta val nt antimonials prepared by Schmidt were tried with varied result between 1916 20 Brahmachari prepared urea stibamine in 1922 and it wa proved to be highly effective Newer antimonials such as

neostibosan solustibosan and *methyl glucamine antimoniate were introduced* subsequently The aromatic diamidines which do not contain antimony were introduced and tested between 1939-49

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION *In the Indo Pakistan subcontinent* kala azar occurs endemically in Assam East Pakistan West Bengal Sikkim Nepal Terais Bihar Uttar Pradesh and Madras The disease is endemic in northern and eastern China and during the last two decades cases have occurred in southern provinces of China *Transcaspia Transcaucasia and Mid Asian republic in the USSR* are areas where kala azar is known to exist Recently indigenous cases have been reported from different parts of Arabia Iran and Asia Minor

In Europe kala azar occurs in Portugal south of Spain and France Italy Sicily Malta Yugo Slavia Greece and Crete *In Africa* the disease is prevalent along the Mediterranean coast excepting Egypt in the Sudan Abyssinia and East Africa Occasional cases have been reported from Central Tropical Africa In South America kala azar is mainly prevalent in Brazil Venezuela and Argentina

✓*It has been noted in India that kala azar is mainly confined to areas* below the altitude of 2000 feet areas with high humidity and low diurnal variation of temperature and to alluvial soil Kala azar is essentially a disease of rural areas and in cities it occurs in areas where conditions resembling those in villages exist It is a house site and *family infection*

AGE AND SEX INCIDENCE In India more than half the cases are between 5 15 years of age In the Mediterranean countries about 90 per cent of the cases occur in infants and small children below the age of 5 years Older age groups are more frequently affected in the Sudan and East Africa In other countries the age incidence is similar to that in India Males are more frequently affected than females

SEASONAL INCIDENCE *In Calcutta cases are seen throughout the* year but the onset of most of the cases is between November and March

CAUSATIVE ORGANISM The protozoan parasite *Leishmania donovani* Laveran & Mesnil 1903 belongs to the family Trypanosomidae and the genus Leishmania It occurs in two forms *viz (a) leishmanial* form *or the Leishman Donovan body* in the cytoplasm of the reticulo-endothelial cells of the human or mammalian host and *(b)* the *leptomonad* or the flagellate form in the insect vector viz the female

and fly of species *Phlebotomus argentipes* in India and in culture in artificial medium

The leishmanial form of *Leishmania donovani* is oval rounded or torpedo-shaped and measures 2 5 *microns* in its maximum diameter It is essentially biconvex in shape with the oval or rounded nucleus of diameter a little over half of that of the parasite itself situated along the more convex border A rod shaped kinetoplast lying tangentially to the nucleus extends to the less convex border of Leishman Donovan body In Leishman or Giemsa stained smears the kinetoplast is stained darker purple than nucleus and the cytoplasm which is stained pale blue shows one or two small vacuoles



FIG 14 Showing *Leishmania donovani* inside a histiocyte A few are also outside the cell

The leptomonad form of *L donovani* is readily obtained by culture of spleen or sternum puncture material in the Nicolle Novy McNeal (N N N) medium incubated between 20 28°C for a week or ten days It is shaped like a cigar or a spindle or it may be more or less pear shaped (Fig 15) Its length varies usually between 10 20 *microns* and the breadth 1 5 3 5 *microns* The nucleus is situated close to the centre of the body and the kinetoplast near the anterior end A flagellum that is about as long as the body of the flagellate arises close to the kinetoplast and extends anteriorly The cytoplasm stains pale blue with Romanowsky stains and may contain a few volutin granules particularly in old culture The flagellate owes its motility to the active movements of the flagellum The leishmanial form which occurs intracellularly is non motile



FIG 15 Leptomonad form of *L donovani*

TRANSMISSION Kala azar is transmitted from infected men suffering from kala azar or possibly post kala azar dermal leishmania is to susceptible individuals by certain species of the sand fly *e g* *Phlebotomus*

argentipes in India In the Mediterranean countries some parts of China and South America dogs or other canines such as the *raposa* in Brazil are regarded as animal reservoir of leishmanial infection

MODE OF INFECTION The female sand fly fed on a case of leishmaniasis ingests the cells containing Leishman Donovan bodies with its blood meal In about a week to ten days there is heavy growth of leptomonads in the mid gut and more anteriorly extending into the proboscis Such heavily infected sand fly when feeding on man introduces a mass of leptomonads into the wound caused by its bite The leptomonads soon lose their flagella and are taken up by histiocytes occurring locally or mobilised in response to the presence of the parasite The parasite (leishmanial form) engulfed into the cytoplasm of the histiocyte now multiplies and causes rupture of the host cell The liberated leishmanias are taken up by other histiocytes in the area and a local focus of infection is produced Sooner or later the parasitised histiocytes pass into general circulation and the process is repeated in the reticulo-endothelial cells of the viscera particularly of the spleen the bone marrow and the liver

PATHOLOGY

The fundamental tissue reaction to leishmanial infection consists of proliferation of histiocytes (*i e* reticulo endothelial cells) which is associated with the increase of lymphocytes and plasma cells The reticulo-endothelial cells being most abundant in the spleen liver and bone marrow the pathological changes are most marked in these organs

SPLEEN It is almost invariably enlarged and in very chronic cases it may weigh as much as 5 6 kilogrammes In an average case it is soft in consistency but in very chronic cases it feels firm The capsule is thickened and perisplenitis may occasionally be present The cut surface dark red in colour tends to bulge out It may appear somewhat depressed in the regions of the malpighian follicles Infarct may occasionally be present

The predominant histological change consists of marked proliferation and parasitisation of the reticulo endothelial cells in the red pulp of the spleen These cells encroach on the malpighian follicles which are usually attenuated as a result There is marked increase and congestion of splenic sinusoids which may contain large phagocytic cells with ingested red and white blood cells and often leishmania as well Numerous lymphocytes and plasma cells are seen in the splenic pulp

in addition to the proliferated and parasitised histiocytes There is increase of supporting connective ti sue

LIVER The liver is usually enlarged It is firm to the feel and on section it appears greasy on account of fatty changes or may even show nut meg appearance in post mortem material Histologically proli feration and swelling of Kupfter cells lining the hepatic sinusoids are een and a fair proportion of these cells is parasitised Foci of parasitised and non parasitised histiocytes lymphocytes and plasma cells may be seen lying in between hepatic parenchyma cells and in the portal tracts The parenchyma cells may show fatty changes and the sinusoids are congested with blood Fibrosis is uncommon in uncomplicated cases of kal i azar

BONE MARROW The yellow marrow in the shafts of the long bones is replaced by red cellular marrow Histologically large number of parasitised histiocytes are seen along with increase of lymphocytes and particularly of plasma cells Hæmopoietic tissue is hyperplastic with marked increase of erythroid cells adequate or reduced myeloid cells and normal megakaryocytes

OTHER TIS UES The parasite has been demonstrated in the lymph glands (frequently in the Sudan type of kala azar) suprarenal cortex testis skin (China and South America) intestinal submucosa etc

CLINICAL MANIFESTATIONS

INCUBATION PERIOD This is usually between 2 6 months but may be a hort as three weeks or as long as about two years In experimental transmission of kala azar to man the incubation period was about 5 months

MODE OF ONSET There are three well recognised modes of onset of kala azar z i malaria lil e enteric like and insidiou

In the cases with malaria like onset there is intermittent fever with chill and rigor that is not affected by quinine or other antimalarials In the second type the disea e begins like an attack of enteric fever the temperature gradually mounting to the fastigium in a week and conti nuing as high remittent pyrexia for a week or ten days and then coming down by lysis the total period of the initial pyrexia being about 3-4 weeks In the ca es with in idious type of onset the patients give a hi tory of in I finite period of ill health pos ibly occa ional attacks of fever lo s of weight anæmia and hows spl nomegaly and other feature of the di ease on examination

FEVER The fever of kala azar is best described as irregular in type It may be high or low continuous remittent or intermittent and there are periods of apyrexia during the course of the disease Enteric like onset is usually followed by a period of apyrexia and then by recurrence of fever which may be remittent or intermittent Periods of apyrexia are noted both in cases with malarial or insidious onset

A type of fever is held to be characteristic of kala azar *viz* the double remittent or intermittent fever (Fig 16)

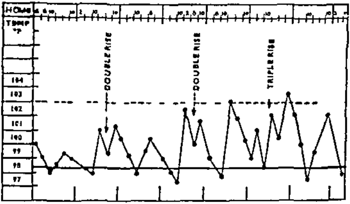


FIG. 16 Temperature chart of kala azar showing double rise

The temperature subsides in the early morning and remains low until about midday It rises in the afternoon subsiding again in the evening At about 8 or 9 p m it rises again or the second rise may *be delayed until midnight and the temperature subsides again* towards morning This is found in about 20 per cent of cases if the temperature is carefully recorded every four hour

One special feature of fever of kala azar is that it is unaccompanied by toxæmia or marked malaise The patient may be going about or doing his work with a fever of 102°F and be quite unaware of his fever

GENERAL APPEARANCE In the advanced stage of kala azar the patient is weak emaciated and anæmic The hair is dry lustreless and scanty The skin is dry and shows increase of pigmentation over the forehead the nose and around the mouth and in occasional cases there may be generalised pigmentation all over the body The abdomen is protuberant with markedly enlarged spleen and liver and occasionally due to ascites as well Cutaneous veins are prominent over the lower part

of the chest and upper part of the abdomen The limbs are miserably thin and there may be some degree of œdema around the ankles (Fig 17)

ALIMENTARY TRACT The tongue is usually clean it may show signs of avitaminosis (B complex) The appetite is good but the digestion may be poor Gingivitis with loosening of the teeth bleeding from the gums may be present frequently Stomatitis leading to *cancrum oris* may appear as a serious complication in chronic cases Diarrhœa or dysentery may be present

SPLEEN The spleen is almost invariably enlarged in kala azar It becomes palpable about the end of the second week of illness and then enlarges progressively By about six months it reaches the umbilicus and in untreated and relapsing cases it may be massively enlarged reaching almost to the pelvis or the right iliac region The spleen is soft in the early stages when it is small in size In late stages it becomes firm but massively enlarged and is usually not tender

LIVER The liver is enlarged in majority of cases (over 80 per cent) Its sharp lower edge is readily palpated and usually it is not tender The left lobe often shows distinct enlargement

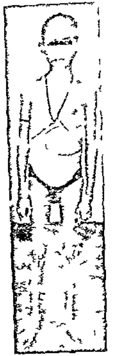


FIG 17 Showing general appearance in advanced stage of kala azar The borders of the enlarged spleen and the liver have been outlined

CIRCULATORY SYSTEM The pulse is often rapid even when the patient is afebrile Systolic bloodpressure is rather low being near about 100 mm of mercury in adults The heart may show slight enlargement and hæmic murmurs may be present Marked carotid pulsation may be present The patient may complain of breathlessness and palpitation on exertion The cardiac symptoms and signs are usually due to anæmia

RESPIRATORY SYSTEM There may be an irritating and troublesome cough due to pressure of the enlarged spleen on the diaphragm Bronchitis may be present and bronchopneumonia lobar pneumonia and pulmonary tuberculosis may occur as serious complications

NERVOUS SYSTEM Symptoms relating to the nervous system are

usually absent in kala azar Headache is uncommon and mental faculties are unimpaired

URINARY SYSTEM Puffiness of the face oedema of the legs and even anasarca may be present but these cases do not usually show any albuminuria or casts in the urine In occasional cases only albumin erythrocytes and granular casts may be present but azotæmia is distinctly uncommon In average cases the urine does not show any abnormality

SKIN AND SUBCUTANEOUS TISSUES The skin is generally very dry and rough and may show accentuation of pigmentation Scabies and impetigo are fairly common

REPRODUCTIVE SYSTEM Amenorrhœa is an early symptom

LYMPHATIC GLANDS Enlargement of lymph glands particularly those in the inguinal region and occasionally in the neck is not uncommon in kala azar in the Sudan and may occasionally be seen in Mediterranean type of the disease This feature is unknown in Indian kala azar

BLOOD Anæmia which is normocytic and orthochromic in the vast majority of cases is a prominent feature in the well developed stage of kala azar It is however not of marked degree in the early stages Hæmoglobin value usually lies between 5 8 g per 100 c cm of blood in the majority of cases and the red cells count between 2 3 million per c mm Severe anæmia with hæmoglobin value lying between 3 4 g *per cent* and the red cell count in the neighbourhood of 1 million per c mm may develop in some cases The anæmia may be microcytic dimorphic or hypochromic in type in relatively smaller proportion of cases

Leucopenia develops early in the disease and is progressive The leucocyte count lies between 1 3 thousand in majority of cases in chronic kala azar In occasional cases leucopenia may progress to agranulocytosis with leucocyte count of 500 to 1000 per c mm with 2 3 per cent or no granulocytes The differential count shows relative and absolute decrease of polymorphonuclear neutrophils and there is relative increase of lymphocytes and monocytes the eosinophils are decreased markedly

The platelet count is usually in the low normal range or below normal Severe thrombocytopenia may occur as a complication of kala azar

BIOCHEMICAL CHANGES There is a profound decrease of serum albumin associated with a very marked increase of *gamma* globulin of

a slower mobility than normal The increase of *gamma* globulin is noted from the early stages of the disease when only the complement fixation test is positive and the aldehyde and the antimony tests are negative Tests of hepatic function *viz* thymol turbidity Takata Ara serum colloidal gold test intravenous hippuric acid test etc indicate defective function of the liver Prothrombin time is also generally increased more in chronic cases than in early ones There is increase of serum bilirubin in about one third of the cases

Evidence of adrenocortical hypofunction is obtained with the help of Cutler Power Wilder test in about half the chronic cases Urinary excretion of 17 ketosteroids is decreased markedly in chronic cases of kala azar this may partly be due to associated malnutrition

COMPLICATIONS

As a result of leucopenia anaemia and malnutrition patients suffering from kala azar are very liable to serious complications caused by various bacterial infections These are classified below

ALIMENTARY SYSTEM (*a*) *Cancrum oris* a condition held as most classical and most fatal in kala azar It affects children more frequently The condition usually starts either near the margins of the gums or the inner aspect of the cheek as an inflammation and soon progresses to necrosis and gangrene which extends to the face In untreated cases extensive sloughing may occur with a fatal termination

(*b*) Severe diarrhœa

(*c*) Dysentery bacillary or amœbic

(*d*) Jaundice

RESPIRATORY SYSTEM (*a*) Bronchitis (*b*) Lobar or bronchopneumonia (*c*) Pulmonary tuberculosis (*d*) Pleurisy empyema

CIRCULATORY SYSTEM (*a*) Cardiac dilatation and rarely cardiac failure and pericarditis (*b*) Oedema ascites and anasarca This is not due to cardiac failure in the vast majority of cases Oedema is noted during the course of kala azar at some time or other in about 40 50 per cent of cases It is mainly due to alteration of serum proteins and lowering of colloidal osmotic pressure of blood Mechanism is somewhat similar to that in hunger œdema

BLOOD (*a*) Grave anæmia (*b*) Agranulocytosis (*c*) Thrombocytopenia with hæmorrhage Hæmorrhage may be of the nature of minute to large petechial spots epistaxis hæmorrhage from the gastrointestinal tract extensive hæmorrhages under the skin and

usually absent in kala azar Headache is uncommon and mental faculties are unimpaired

URINARY SYSTEM Puffiness of the face œdema of the legs and even anasarca may be present but these cases do not usually show any albuminuria or casts in the urine In occasional cases only albumin erythrocytes and granular casts may be present but azotæmia is distinctly uncommon In average cases the urine does not show any abnormality

SKIN AND SUBCUTANEOUS TISSUES The skin is generally very dry and rough and may show accentuation of pigmentation Scabies and impetigo are fairly common

REPRODUCTIVE SYSTEM Amenorrhœa is an early symptom

LYMPHATIC GLANDS Enlargement of lymph glands particularly those in the inguinal region and occasionally in the neck is not uncommon in kala azar in the Sudan and may occasionally be seen in Mediterranean type of the disease This feature is unknown in Indian kala azar

BLOOD Anæmia which is normocytic and orthochromic in the vast majority of cases is a prominent feature in the well developed stage of kala azar It is however not of marked degree in the early stages Hæmoglobin value usually lies between 5 8 g per 100 c cm of blood in the majority of cases and the red cells count between 2 3 million per c mm Severe anæmia with hæmoglobin value lying between 3-4 g per cent and the red cell count in the neighbourhood of 1 million per c mm may develop in some cases The anæmia may be macrocytic dimorphic or hypochromic in type in relatively smaller proportion of cases

Leucopenia develops early in the disease and is progressive The leucocyte count lies between 1 3 thousand in majority of cases in chronic kala azar In occasional cases leucopenia may progress to agranulocytosis with leucocyte count of 500 to 1000 per c mm with 2 3 per cent or no granulocytes The differential count shows relative and absolute decrease of polymorphonuclear neutrophils and there is relative increase of lymphocytes and monocytes the eosinophils are decreased markedly

The platelet count is usually in the low normal range or below normal Severe thrombocytopenia may occur as a complication of kala azar

BIOCHEMICAL CHANGES There is a profound decrease of serum albumin associated with a very marked increase of *gamma* globulin of

DIAGNOSIS

The diagnosis of kala azar depends on (*a*) clinical feature (*b*) serum tests and (*c*) demonstration of the parasite *Leishmania donovani*

A In the early stages of the disease *i e* during the first four weeks the following features are suggestive

CLINICAL DATA 1 History of residence in an endemic area and of any other member of the family having kala azar

2 Remittent or intermittent fever with a double rise in twenty four hours

3 Lack of toxemia

4 Presence of clean tongue good appetite and lack of gastro intestinal complications

5 Soft enlargement of the spleen felt about the third week and not associated with pain or tenderness on palpation

6 Liver just palpable

7 Lack of response to antimalarials or antibiotic treatment for enteric fever

LABORATORY DATA Moderate leucopenia (3 4 000) with relative decrease of neutrophils

Of the serum tests only the complement fixation test with an antigen prepared from certain acid fast bacilli particularly Kedrowsky s acid fast bacillus is of value It becomes positive from the third week of illness

The parasite is best demonstrated by examination of smears from material obtained by sternal iliac or tibial puncture Culture of the same in N N N medium is also useful provided contamination can be avoided Liver puncture and culture are also useful The spleen is usually too small for satisfactory puncture at this stage

B In the chronic or well developed stage *i e* after three months of illness the following additional data are of value

CLINICAL DATA 1 Mode of onset and subsequent course of fever particularly relapse after a period of apyrexia the fever during relapse being more irregular or showing characteristic double rise than during the initial attack

2 Progressive enlargement of the spleen which is soft when the enlargement is not too great

3 Enlargement of the liver particularly when its left lobe appears to overlap the enlarged spleen

mucous membrane internally This may be due to thrombocytopenia hypoprothrombinæmia and may be associated with jaundice (*d*) Retinal hemorrhage alone this may be noted in untreated cases and during treatment

SEPTIC AND INFLAMMATORY CONDITIONS These may affect the mouth and ears and extension of sepsis from the latter (mastoid abscess) may lead to intracranial infection (meningitis)

GENITAL SYSTEM Noma of the vulva of cervix uteri

URINARY SYSTEM In rare cases nephritis

SKIN (*a*) Scabies and impetigo are common in chronic case (*b*) Herpes zoster may develop during antimony treatment

COURSE

In the pre antimony days the vast majority of cases went on to fatal termination within about two years during which they had recurring pyrexial periods with intermissions massive splenomegaly anæmia œdema etc and developed serious and often fatal complications It is held that about 10 25 per cent of cases of kala azar undergo spontaneous cure (see under post kala azar dermal leishmaniasis)

PROGNOSIS

Specific treatment with pentavalent antimonials usually results in cure of about 90 per cent of cases A proportion of cases does not respond to treatment or relapses after an apparent cure Majority of such cases can be cured with the most effective aromatic diamidine compounds But even then a small proportion of cases proves entirely resistant to chemotherapy Mortality rate during treatment varies from 5 15 per cent the larger proportion dying during epidemics than between them

Serious and often fatal complications such as cancrum oris pneumonia dysentery have generally lost their terrors at the present time But the presence of extensive hæmorrhages associated with thrombocytopenia and/or jaundice or of agranulocytosis should be regarded as indicating bad prognosis

Relapses occur in some 8 10 per cent of cases within six months of apparent cure Such cases often require prolonged chemotherapy and some of these may prove drug resistant until splenectomy is done *Outlook is relatively unfavourable in resistant* cases

with the stylet in position and the adjustable stop fixed about ¼ inch from the end of the needle is pushed through the anæsthetized area till the marrow cavity is reached when the stylet is withdrawn Numerous special needles have been introduced for this purpose The most popular one in our country is the Salah needle A dry sterilised 5 c cm Record syringe is fitted to the needle and about ¼ c cm of marrow fluid is aspirated by gentle suction The patient may at this stage complain of some pain Smears from this material are made on half a dozen clean glass slides stained and examined for *L donovani* The site of puncture is sealed with cotton wool soaked in the compound tincture of benzoin

Spleen Puncture 1 *Preparation of the patient* On the night before the operation 30 grains of calcium lactate or gluconate are given Next morning another dose is given ½ to 1 hour before the operation The patient may have a cup of milk and toast early in the morning

2 *Requirements* (i) A tightly fitting 5 or 10 c cm glass syringe with a sharp needle 1½ inches in length

If a culture is to be made oil sterilisation is preferable but if direct smears only the needle is sterilised in boiling oil and the syring in alcohol For smear examination the syringe and the needle should be absolutely dry

(ii) Glass slides and culture tubes

3 *Operation* (i) Patient lies flat on his back near one edge of the bed without pillows and with his left hand underneath the head

(ii) Operator sits on the left side and an assistant from the right side of the patient fixes the spleen with his hand placed below the organ If Napier's spleen puncture syringe is employed the operator fixes the lower pole of the spleen with the left hand and does the puncture with the syringe held in his right hand

(iii) Point of puncture is ½ to 1 inch below the costal margin midway between the anterior and posterior borders of the spleen The skin over the part is first painted with liq iodine and then the point of puncture may be touched with a small drop of pure phenol which is wiped off after a minute with alcohol before the actual puncture

(iv) The operator first punctures the skin obliquely the direction of the needle being upward and inward parallel to costal margin The direction is then changed and the needle is held pointing outward and upward parallel to the long axis of the spleen at 45° angle with the surface The patient is asked to hold his breath and the needle is

4 Comparative sense of well being inspite of prolonged illness
5 Good appetite
6 Hair changes viz thin dry and lustreless
7 Accentuation of pigmentation and dryness of the skin
8 Rapid pulse even when apyrexial

LABORATORY DATA Anæmia leucopenia with decrease of neutrophil and at times thrombocytopenia Leucopenia is progressive and marked The white blood cell count lies between 1 3 000 in over 90 per cent of cases of chronic kala azar There is a relative decrease of polymorphonuclear cells and the eosinophils are markedly decreased or even absent

Decrease of serum albumin with gross increase of globulin

The serum tests of value are (i) the aldehyde test which usually becomes positive after three months of illness (ii) the antimony test which shows positive reaction about 2 3 months after onset and (iii) the complement fixation test

The parasite is most readily demonstrated in spleen puncture smear and culture 95 per cent of cases showing the parasite in the smear Examination of smears of bone marrow shows the L D bodies in about 89 per cent of cases and liver puncture smear in about 80 per cent of cases

The sternal puncture is undoubtedly a valuable method of diagnosis which has of late largely replaced the spleen puncture but is not so certain a method as the latter So cases where the sternal puncture gives negative results should be investigated by spleen puncture

It is possible to demonstrate the parasite in the peripheral blood of the patients with chronic kala azar in a relatively small proportion of cases after very thorough examination and culture may yield the parasite in most cases But the results with bone marrow or splenic smear examination are much more satisfactory and examination of blood smears and culture of blood for *L donovani* are not employed any longer in the diagnosis of kala azar

METHODS OF PUNCTURE *Sternal Puncture* This method is much simpler and safer than spleen puncture and may be used for ambulant patients The patient lies on his back the skin of the mid sternal region at the level of the second intercostal space is painted with liquor of iodine and the site of puncture is anæsthetised down to the periosteum with 2 c cm of 2 per cent novocain solution After proper sterilisation a special short stout needle of the lumbar puncture type

Negative { (−) Solid but transparent
− Serum fluid and unchanged

The final reading is taken after 24 hours unless the serum turns solid and opaque earlier

The aldehyde test is positive in about 74 per cent of all cases of kala azar (*Napier*)

(*b*) *Chopra's Antimony Test* One or two drops of freshly prepared 4 per cent urea stibamine solution in distilled water is added to the patient's serum (diluted 1 in 10 with distilled water) in a Dreyer's tube (narrow test tube) A positive (+) reaction is indicated by a heavy flocculent precipitate appearing immediately and settling in almost half an hour In doubtful reaction (±) the precipitate is fine granular and settles down slowly and if no precipitate occurs the reaction is negative (−) This test however is less reliable than the aldehyde test because it may be positive in cases of splenomegaly not due to kala azar

(*c*) *Brahmachari's Globulin Precipitation Test* To ½ c cm of patient's serum in a test tube is slowly added 1 c cm of distilled water a white ring forms at the junction of the two fluids The test is not positive in early cases of kala azar

(*d*) *The Complement Fixation Test* (*i*) *With an antigen prepared from Kedrowsky's acid fast bacillus* This test has been found to be positive in 95 per cent of cases of kala azar from the third week of illness when all other tests for the disease are negative Positive reaction may be obtained in about 10 per cent of cases of tuberculous disease 5 per cent of cases of eosinophilic lungs 14 per cent of cases of dermal leishmanoid and some cases of lepromatous leprosy

(*ii*) *With antigen prepared from Leishmania infected tissue or culture of L donovani* The former antigen has been reported as satisfactory by Chinese workers and latter by workers in India Both need further controlled study for proper assessment of their diagnostic value

CULTURE FOR LEPTOMONAD FORM OF L DONOVANI Culture of material obtained by bone spleen or liver puncture or of blood in slightly acidified N N N medium (*p*H 6 4) incubated at 22°C for about 10 days may yield positive results in most cases In some cases of blood culture a positive result may be obtained after incubation for as late as one month

rapidly plunged into the spleen The piston is withdrawn quickly 2 or 3 times and the needle taken out immediately The final step of the operation does not take more than 3 or 4 seconds

The contents of the syringe are first squirted on a clean slide and smears made The rest of the contents are washed out with sterile citrated saline into culture tubes of N N N medium

4 *After treatment* (i) A tight abdominal bandage is applied over the spleen to limit the movement of the organ and to stop possible hæmorrhage by direct pressure A dose of gr 30 of calcium lactate or gluconate is then given by the mouth

(ii) The patient should be kept lying in bed for a day He may take his food after 1 or 2 hours Although the operation is perfectly safe in skilled hands (no mortality in a series of 7 000 operations by Napier) a few fatalities have been reported So it should not be undertaken by the inexperienced light heartedly

5 *Contraindications to spleen puncture* (a) Hæmophilia and purpura (b) Jaundice (c) Chronic bronchitis with severe persistent cough (d) Diarrhœa (e) Ascites

Examination of liver puncture material for the *Leishmania donovani* was used at one time in those cases where the spleen was not palpable It is not safer than spleen puncture Besides the results are not better than sternum or spleen puncture

The puncture of the iliac crest is advocated by many The head of the tibia may be punctured in children

SERUM TESTS (a) *Napier's Aldehyde Test* 1 c cm of clear serum is taken in a test tube and one or two drops of commercial formalin (40 per cent solution of formaldehyde) are added to it and the serum is then well shaken Positive reaction is indicated by the serum becoming completely opaque and white The following results may be obtained

Positive	+ + +	Solid and completely opaque in 20 mins
	+ +	2 hours
	+	24 hours
Doubtful	(+)	Solid and milky looks opaque in ordinary light but shows the shape of a window when held up against light
	±	Solid and slightly milky but transparent when held up against light

impulse to the opposite side (*e*) Absence of enlargement of spleen and liver though sometimes they may be displaced downward by the presence of the pleural fluid (*f*) Slight or moderate leucocytosis (*g*) Skiagram shows the characteristic opaque shadow over the costophrenic angle and the lung base with a concave upper border the highest point of which reaches the mid axillary line (*h*) Exploratory puncture shows the presence of fluid

7 *Amœbic Liver Abscess* (*a*) Presence of rigor and sweating associated with spiky rise of temperature (*b*) Rapidly developing anæmia (*c*) Presence of anorexia (*d*) Enlarged and tender liver occasionally with a localised swelling (*e*) Leucocytosis with a comparatively low proportion of the polymorphs (*f*) Positive findings in stools (*g*) X rays show raising of the right dome of the diaphragm limitation of its movement and occasionally filling up of the cardiohepatic angle

8 *Acute Bacterial Endocarditis* (*a*) Presence of rigor sweating and anorexia (*b*) Presence of toxæmia with pain and swelling of joints (*c*) Signs of endocarditis (*d*) Occurrence of embolic phenomena (*e*) Moderate or high leucocytosis (*f*) Detection of causative organisms such as *Streptococcus β hæmolyticus* or *D pneumoniæ* on blood culture

CHRONIC KALA AZAR has to be distinguished from the following

A I Conditions chiefly associated with splenomegaly

1 *Chronic Malaria* (*a*) Anæmia less marked than in chronic kala azar of same duration (*b*) Liver is not often enlarged (*c*) Sudden high rise of temperature with rigor showing tertian or quartan periodicity (*d*) Coated tongue with bad appetite (*e*) Spleen enlarged and hard (*f*) Presence of malaria parasites in blood and hæmozoin pigment in the leucocytes (*g*) Response to adequate antimalarial therapy

2 *Tropical Splenomegaly* (see under Tropical Splenomegaly)

3 *Splenic Anæmia* (*a*) Extraordinary chronic course continuing for 10 or 12 years (*b*) Ascites and jaundice much more common than in kala azar (*c*) Severe anæmia (*d*) Hæmatemesis

4 *Chronic Leukæmias* (*a*) Hard consistency of the enlarged spleen and liver (*b*) Enlargement of lymph glands may be present (*c*) Enormous increase in the number of white cells with appearance of immature white cells in the blood The latter feature clinches the

DIFFERENTIAL DIAGNOSIS

KALA-AZAR IN THE EARLY STAGE should be diagnosed from the following —

1 *Acute Malaria* (*a*) Presence of a tertian or quartan periodicity in the temperature curve (*b*) Frequent occurrence of rigor sweating and vomiting (*c*) Presence of pallor anæmia and jaundice (*d*) Presence of coated tongue and anorexia (*e*) Enlargement of the spleen during the febrile paroxysm and its diminution during the apyrexial period (*f*) Presence of malaria parasites in peripheral blood films (*g*) Prompt response to adequate anti malarial therapy

2 *Enteric Group of Fevers* (*a*) Presence of toxæmic signs and symptoms (*b*) Presence of heavily coated tongue with anorexia distended abdomen diarrhœa and sometimes hæmorrhage from the bowel (*c*) Relative bradycardia and occasional dicrotism (*d*) Presence of rose spots (*e*) Blood culture shows *S typhi S paratyphi A* or *B* (*f*) Positive Widal's test

3 *Esch coli Infection of the Urinary Tract* (*a*) Presence of rigor and sweating associated with a spiky rise of temperature (*b*) Frequent micturition with pain and tenderness in the loins (*c*) Presence of leucocytosis (*d*) Positive urinary findings (Turbidity fishy odour numerous pus cells and culture positive)

4 *Pulmonary Tuberculosis* (*a*) History of cough hæmoptysis and pleural effusion (*b*) Irregular rise of temperature (*c*) Presence of toxæmic symptoms such as anorexia nausea tachycardia (*d*) Positive lung findings (*e*) Positive sputum and X ray findings

5 *Acute Miliary Tuberculosis* (*a*) Irregular or typhoid like temperature chart (*b*) Presence of marked toxæmia associated with malar flush night sweats rapid wasting mental apathy stupor or muttering delirium (*c*) Signs of diffuse bronchitis or bronchopneumonia with cyanosis and dyspnœa (*d*) Choroidal tubercles may be found on ophthalmoscopic examination (*e*) Presence of *M tuberculosis* occasionally on sputum examination (*f*) Characteristic fine diffuse mottling of the lungs shown by a skiagram

6 *Small Pleural Effusion* (*a*) Onset of fever with dry cough and pain in one side of the chest (*b*) Presence of anorexia (*c*) Localising lung signs such as diminished movement slight fulness of the lower intercostal spaces stony resistant dulness on percussion, diminution or absence of vocal fremitus breath sounds and vocal resonance on the affected side (*d*) Slight displacement of cardiac

impulse to the opposite side (*e*) Absence of enlargement of spleen and liver though sometimes they may be displaced downward by the presence of the pleural fluid (*f*) Slight or moderate leucocytosis (*g*) Skiagram shows the characteristic opaque shadow over the costophrenic angle and the lung base with a concave upper border the highest point of which reaches the mid axillary line (*h*) Exploratory puncture shows the presence of fluid

7 *Amœbic Liver Abscess* (*a*) Presence of rigor and sweating associated with spiky rise of temperature (*b*) Rapidly developing anæmia (*c*) Presence of anorexia (*d*) Enlarged and tender liver occasionally with a localised swelling (*e*) Leucocytosis with a comparatively low proportion of the polymorphs (*f*) Positive findings in stools (*g*) X rays show raising of the right dome of the diaphragm limitation of its movement and occasionally filling up of the cardio hepatic angle

8 *Acute Bacterial Endocarditis* (*a*) Presence of rigor sweating and anorexia (*b*) Presence of toxæmia with pain and swelling of joints (*c*) Signs of endocarditis (*d*) Occurrence of embolic phenomena (*e*) Moderate or high leucocytosis (*f*) Detection of causative organisms such as *Streptococcus β hæmolyticus* or *D pneumoniæ* on blood culture

CHRONIC KALA AZAR has to be distinguished from the following

A I Conditions chiefly associated with splenomegaly

1 *Chronic Malaria* (*a*) Anæmia less marked than in chronic kala azar of same duration (*b*) Liver is not often enlarged (*c*) Sudden high rise of temperature with rigor showing tertian or quartan periodicity (*d*) Coated tongue with bad appetite (*e*) Spleen enlarged and hard (*f*) Presence of malaria parasites in blood and hæmozoin pigment in the leucocytes (*g*) Response to adequate anti malarial therapy

2 *Tropical Splenomegaly* (see under Tropical Splenomegaly)

3 *Splenic Anæmia* (*a*) Extraordinary chronic course continuing for 10 or 12 years (*b*) Ascites and jaundice much more common than in kala azar (*c*) Severe anæmia (*d*) Hæmatemesis

4 *Chronic Leukæmias* (*a*) Hard consistency of the enlarged spleen and liver (*b*) Enlargement of lymph glands may be present (*c*) Enormous increase in the number of white cells with appearance of immature white cells in the blood The latter feature clinches the

DIFFERENTIAL DIAGNOSIS

KALA-AZAR IN THE EARLY STAGE should be diagnosed from the following —

1 *Acute Malaria* (*a*) Presence of a tertian or quartan periodicity in the temperature curve (*b*) Frequent occurrence of rigor sweating and vomiting (*c*) Presence of pallor anæmia and jaundice (*d*) Presence of coated tongue and anorexia (*e*) Enlargement of the spleen during the febrile paroxysm and its diminution during the apyrexial period (*f*) Presence of malaria parasites in peripheral blood films (*g*) Prompt response to adequate anti malarial therapy

2 *Enteric Group of Fevers* (*a*) Presence of toxæmic signs and symptoms (*b*) Presence of heavily coated tongue with anorexia distended abdomen diarrhœa and sometimes hæmorrhage from the bowels (*c*) Relative bradycardia and occasional *dicrotism* (*d*) Presence of rose spots (*e*) Blood culture shows *S typhi S paratyphi A* or *B* (*f*) Positive Widal s test

3 *Esch coli Infection of the Urinary Tract* (*a*) Presence of rigor and sweating associated with a spiky rise of temperature (*b*) Frequent micturition with pain and tenderness in the loins (*c*) Presence of leucocytosis (*d*) Positive urinary findings (Turbidity fishy odour numerous pus cells and culture positive)

4 *Pulmonary Tuberculosis* (*a*) History of cough hæmoptysis and pleural effusion (*b*) Irregular rise of temperature (*c*) Presence of toxæmic symptoms such as anorexia nausea tachycardia (*d*) Positive lung findings (*e*) Positive sputum and X ray findings

5 *Acute Miliary Tuberculosis* (*a*) Irregular or typhoid like temperature chart (*b*) Presence of marked toxæmia associated with malar flush night sweats rapid wasting mental apathy stupor or muttering delirium (*c*) Signs of diffuse bronchitis or broncho pneumonia with cyanosis and dyspnœa (*d*) Choroidal tubercles may be found on ophthalmoscopic examination (*e*) Presence of *M tuberculosis* occasionally on sputum examination (*f*) Characteristic fine diffuse mottling of the lungs shown by a skiagram

6 *Small Pleural Effusion* (*a*) Onset of fever with dry cough and pain in one side of the chest (*b*) Presence of anorexia (*c*) Localising lung signs such as diminished movement slight fulness of the lower intercostal spaces stony resistant dulness on percussion, diminution or absence of vocal fremitus breath sounds and vocal resonance on the affected side (*d*) Slight displacement of cardiac

impulse to the opposite side (*e*) Absence of enlargement of spleen and liver though sometimes they may be displaced downward by the presence of the pleural fluid (*f*) Slight or moderate leucocytosis (*g*) Skiagram shows the characteristic opaque shadow over the costophrenic angle and the lung base with a concave upper border the highest point of which reaches the mid axillary line (*h*) Exploratory puncture shows the presence of fluid

7 *Amœbic Liver Abscess* (*a*) Presence of rigor and sweating associated with spiky rise of temperature (*b*) Rapidly developing anæmia (*c*) Presence of anorexia (*d*) Enlarged and tender liver occasionally with a localised swelling ( ) Leucocytosis with a comparatively low proportion of the polymorphs (*f*) Positive findings in stools (*g*) X rays show raising of the right dome of the diaphragm limitation of its movement and occasionally filling up of the cardiohepatic angle

8 *Acute Bacterial Endocarditis* (*a*) Presence of rigor sweating and anorexia (*b*) Presence of toxæmia with pain and swelling of joints (*c*) Signs of endocarditis (*d*) Occurrence of embolic phenomena (*e*) Moderate or high leucocytosis (*f*) Detection of causative organisms such as *Streptococcus β hæmolyticus* or *D pneumoniæ* on blood culture

CHRONIC KALA AZAR has to be distinguished from the following

A I Conditions chiefly associated with splenomegaly

1 *Chronic Malaria* (*a*) Anæmia less marked than in chronic kala azar of same duration (*b*) Liver is not often enlarged (*c*) Sudden high rise of temperature with rigor showing tertian or quartan periodicity (*d*) Coated tongue with bad appetite (*e*) Spleen enlarged and hard (*f*) Presence of malaria parasites in blood and hæmozoin pigment in the leucocytes (*g*) Response to adequate anti malarial therapy

2 *Tropical Splenomegaly* (see under Tropical Splenomegaly)

3 *Splenic Anæmia* (*a*) Extraordinary chronic course continuing for 10 or 12 years (*b*) Ascites and jaundice much more common than in kala azar (*c*) Severe anæmia (*d*) Hæmatemesis

4 *Chronic Leukæmias* (*a*) Hard consistency of the enlarged spleen and liver (*b*) Enlargement of lymph glands may be present (*c*) Enormous increase in the number of white cells with appearance of immature white cells in the blood The latter feature clinches the

diagnosis even in the aleukæmic phase occurring spontaneously or as result of irradiation (*d*) Characteristic myelogram

5 *Portal Cirrhosis* (*a*) Muddy yellow tint of the emaciated face (*b*) Enlargement of the spleen is slight or moderate (*c*) Presence of ascites and jaundice (*d*) Liver is often not palpable

6 *Hodgkin's Disease* (*a*) Characteristic painless enlargement of the lymph glands specially of the neck (*b*) Spleen neither so much enlarged nor soft and smooth as in kala azar (*c*) Presence of moderate leucocytosis with slight eosinophilia (*d*) All the laboratory tests for kala azar are negative (*e*) Demonstration of the characteristic histological picture by biopsy of the lymph node

7 *Acholuric Jaundice* (*a*) History of repeated attacks of hæmolytic type of jaundice since childhood (*b*) Absence of hepatic enlargement (*c*) Increased fragility of the red cells hæmolysis beginning at 0 6 per cent and complete at 0 42 per cent sodium chloride solution

8 *Polycythæmia Vera* (*a*) The characteristic plum coloured appearance (*b*) The hard enlarged spleen (*c*) Hypertension in Gaisbock's type (*d*) Polycythæmia with 7-12 million of red cells per c mm (*a*) Moderate leucocytosis

9 *Gaucher's Splenomegaly* (*a*) Very rare (*b*) A very chronic course of 10-20 years or even more associated with a fair health (*d*) Presence of pinguecula in the eyes (*d*) Presence of slight anæmia ( ) Presence of the characteristic large foamy cells in smears from sternal puncture material

10 *Trypanosomiasis* (*a*) It does not occur in India (*b*) Generalised enlargement of the lymph nodes which are at first painless but later on painful (*c*) Transient erythematous rash on trunk (*d*) Muscular weakness with mental apathy drowsiness and even coma in the later stages (*e*) Presence of trypanosomes in the peripheral blood and gland puncture material and in the cerebrospinal fluid in the later stages

11 *Hydatid Cyst of the Spleen* (*a*) History of repeated attacks of perisplenitis (*b*) Presence of fluctuation in the splenic tumour (*c*) Presence of eosinophilia (*d*) Positive Casoni test in 90 per cent of cases

12 *Visceral Bilharziasis* (*a*) Occurs in upper and lower Egypt (*b*) Cirrhosis of liver and ascites common in later stages (*c*) Protracted course (*d*) Blood changes initial leucocytosis with myelocytes in peripheral blood and eosinophilia later leucopenia marked anæmia (*e*) Eggs in fæces or in scraping or biopsy after sigmoidoscopy (*f*) Positive complement fixation and intradermal test for bilharziasis

II Splenomegalic conditions in childhood

1 *Biliary Cirrhosis* (*a*) History of a previous case in the family is significant (*b*) Irregular fever with progressive enlargement of liver first and later of spleen (*c*) Presence of jaundice—*an important*

feature (*d*) Occurrence of ascites (*e*) Slight or moderate leucocytosis (*f*) Negative laboratory tests for kala azar

2 *Rickets* (*a*) Fat flabby and pale appearance (*b*) Sweating of the head at night (*c*) Bossed head due to marked thickening of the frontal and parietal eminences (*d*) Presence of beadings at the costo-chondral junctions (rickety rosary) (*e*) Enlargement of the epiphyses at the wrists and ankles and bowing of the tibiæ (*f*) Splenomegaly slight or moderate

3 *Congenital Syphilis* (*a*) The syphilitic facies with depressed bridge of the nose radiating scars from the angles of the mouth and corneal opacities (*b*) Notching of the upper central permanent incisors (Hutchinson s teeth) and pitted dome shaped Moon s molars may be present (*c*) Liver is enlarged and may be irregular (*d*) Presence of sabre shaped tibiæ (*e*) Positive Wassermann reaction

4 *Lymphatic Leukæmia* (*a*) Generalised enlargement of the superficial lymph glands (*b*) Hemorrhages into the skin subcutaneous tissues and muscles and from the mucous membranes (*c*) A very high leucocytosis with increase of small lymphocytes up to 90 95 per cent (*d*) Characteristic myelogram

5 *Von Jaksch s Anæmia* (*a*) Onset usually before 5 years of age (*b*) Slight enlargement of the superficial lymph nodes may be present (*c*) Hard consistency of the enlarged spleen (*d*) Hypochromic microcytic anæmia with many normoblasts in the peripheral blood (*e*) Moderate leucocytosis with constant presence of myelocyte 10 25 per cent

6 *Cooley s Anæmia* (*a*) Occurs usually in children (*b*) Familial incidence is usually seen (*c*) Hard splenic enlargement (*d*) Hypochromic anæmia with normoblasts neutrophilic myelocytes and target cells in the peripheral blood The red cells are unduly resistant to hypotonic salt solution (*e*) X ray examination shows widening of the medullary portion of the bones thinning of the cortex and characteristic vertical striations in the skull bones

7 *Still s Disease* (*a*) Presence of pain and swelling in the small joints of the hands and feet and also in wrist ankle and knee (*b*) Enlargement of the superficial lymph nodes in the neck and epitrochlear regions (*c*) Moderate leucocytosis

The differentiation of chronic kala azar in childhood from splenic anæmia Hodgkin disease and acholuric jaundice is the same as in adults

B Conditions associated with marked anæmia generalised œdema and ascites

1 *Severe Anæmia of Hookworm Infestation* (*a*) The characteristic pale white flabby tongue (*b*) Absence of splenic enlargement (*c*) Presence of eosinophilia (*d*) Presence of hookworm ova in the stool

2 *Subacut Nephritis* (*a*) Presence of oliguria and albuminuria with a large number of hyaline granular fatty and epithelial casts (*b*) Absence of splenic enlargement (*c*) Liver usually not enlarged unless there is associated congestive cardiac failure (*d*) Evidences of cardiac enlargement arterial thickening increased bloodpressure retinal changes increased non protein nitrogen may be present specially in the late stage

3 *Portal Cirrhosis* (see page 68)

4 *Splenic Anæmia* (see page 68)

5 *Tuberculous Peritonitis* (*a*) Evidence of tuberculous disease in other parts of the body such as lungs pleuræ lymph nodes and intestines (*b*) Presence of ascites with irregular masses in the abdominal cavity (*c*) Presence of some tenderness all over the abdomen with red and indurated umbilicus

6 *Malignant Disease of the Peritoneum* (*a*) Evidence of malignant disease in the stomach rectum pancreas gallbladder liver breast ovary or testicle (*b*) Presence of enlarged lymph glands and nodular masses in the abdomen near about the epigastrium or the umbilicus (*c*) Absence of splenic enlargement

C Conditions associated with recurrent attacks of pyrexia

1 *Hodgkin s Disease* (see page 68)

2 *Subacut Bacterial Endocarditis* (*a*) Presence of toxæmia (*b*) Evidence of valvular disease or congenital heart disease (*c*) Occurrence of embolic phenomena (*d*) Clubbing of fingers (*e*) Moderate leucocytosis (*f*) Positive blood culture

3 *Undulant Fever* (*Malta Fever*) (*a*) Rare in India except in the Punjab (*b*) Occurrence of pain and swelling in the joint (*c*) Presence of intercostal and sciatic neuralgia (*d*) Presence of coated tongue and bad appetite (*e*) Leucocyte count is usually normal (*f*) Positive agglutination test with *Br melitensis* in a dilution of 1 in 100 or more (*g*) Positive blood culture

TREATMENT

GENERAL MANAGEMENT

During the stage of fever the patient must have complete rest in bed. Mouth should be scrupulously kept clean by the use of antiseptic washes such as hydrogen peroxide and boro glycerine. Bowels should be attended to.

Diet. The kala azar patient has usually a good appetite and hence a liberal diet adequate in calories and high in protein and vitamin C content should be given unless contraindicated by hyperpyrexia, dysentery or diarrhoea. The diet should consist of milk, bread, butter, lightly boiled eggs, soft rice, mashed potato, boiled vegetables, fish, minced meat, stewed chicken, *dals* and fruits.

SPECIFIC TREATMENT

Antimony preparations are specific in the treatment of this disease. More recently some aromatic diamidines have also been found to be effective.

Indications and contraindications for antimonials and aromatic diamidines. The pentavalent antimony compounds are generally used for the treatment of kala azar unless it is complicated by tuberculous disease. The cases with pneumonia, dysentery, haemorrhage, jaundice, signs of renal damage are treated with antimonials but only when the acute conditions like pneumonia or dysentery have subsided. The aromatic diamidine compounds are used for the treatment of antimony resistant cases, the cases showing hypersensitive reaction to antimony and those complicated with tuberculous disease. The aromatic diamidine compounds are not generally used in cases showing evidence of serious hepatic or renal damage or haemorrhages because of their potential toxic action on the liver and the kidneys.

ANTIMONY PREPARATIONS. A. TRIVALENT COMPOUNDS. ANTIMONYL TARTRATES. Intravenous injection of tartar emetic (potassium antimonyl tartrate) was started in 1915 by Di Cristina and Caronia in infantile kala azar with satisfactory results. Then Rogers, Muir, Knowles and Brahmachari tried this drug in the treatment of Indian kala azar with singular success.

Later on a freshly prepared 2 per cent solution of sodium antimonyl tartrate was used intravenously on alternate days beginning with 2 c.cm. in the adult and increasing each subsequent dose by 1 c.cm. till a maximum dose of 5 c.cm. was reached and the injections were continued till a total dose of 2.5 to 4 g. of the drug

was administered in course of about 3 months But because of many disadvantages of this mode of treatment their general use has been abandoned since the introduction of less toxic pentavalent compounds

B PENTAVALENT COMPOUNDS The discovery of the pentavalent antimony compounds has however opened a new era in the treatment of kala azar These compounds are more parasitotropic and less organotropic There is now a large number of such organic compounds of antimony available in the market viz urea stibamine (*Brahmachari*) amino stiburea neostibo an solu stibosan stibatin and a host of other

UREA STIBAMINE (Urea para aminophenylstibinic acid) Antimony content is about 35 per cent This drug was introduced by Brahmachari in 1922 It is available as a soluble powder in sealed ampoules in the following graduated doses—0 05 g 0 1 g 0 15 g and 0 2 g

Preparation of the solution A solution of 5 per cent strength in *double distilled water at room temperature should be freshly prepared* for the injection

Mode of administration The injection should always be given intravenously

Dose For adults the injection is started with 0 05 g and increased by 0 05 g till the maximum dose of 0 2 g is reached and it is repeated in subsequent injections The injections should be given every alternate day or thrice a week The total dose to effect a cure is about 2 7 g in 15 injections for an adult

For children of 5 years the initial dose is 0 05 g and it i increased up to 0 1 g The initial dose for older children is 0 05 g the maximum 0 15 g and the total dose 2 1 g

Advantages 1 Rapid clinical improvement within as short a period as 1 2 weeks Immediate cure rate goes up to 90 to 95 per cent 2 Toxic symptoms are rare 3 Infrequency of symptoms of intolerance 4 Rarity of relapses (about 5 per cent)

NEOSTIBENE It is available as a powder in sealed ampoules along with a special solvent in separate ampoules in graduated doses—0 05 g 0 1 g 0 15 g and 0 2 g The freshly prepared solution is injected intramuscularly It is however more painful than neostibosan

NEOSTIBOSAN (Di ethyl amine para aminophenyl stibinate) It contains 42 per cent of metallic antimony in the pentavalent form It is also available in ampoules as an easily soluble yellow powder in the following doses—0 05 g 0 1 g 0 2 g and 0 3 g

Preparation of the solution A 5 to 25 per cent solution is always freshly prepared in sterile distilled water

Mode of administration The 5 per cent solution is given intravenously whereas the 25 per cent solution is injected intramuscularly

Dose In the case of adults the initial dose is 0 2 g and subsequent doses are 0 3 g each The children require a relatively larger dose than adults and tolerate it well

The injections are given daily or on alternate days 12 injections (a total of 3 to 4 g) are given as a routine The immediate response to treatment is not so important as the condition of the patient three weeks after the completion of the treatment

Advantages 1 Rapid improvement of the clinical condition 2 Apparent cure in 3 4 weeks 3 Symptoms of toxicity and intolerance are rare 4 Relapses are few (about 5 per cent) 5 It can be given by the intramuscular route which is the method of choice in cases of children

SODIUM STIBOGLUCONATE (*Conc stibatin stibinol*–100 *stibanate solustibosan pentostam*) The compound was introduced by Kikuth and Schmidt as solustibosan At the present time it is supplied as ready made solution containing 100 mg of antimony per c cm The solution is stable and the compound the least toxic of the pentavalent antimonials

Mode of administration It is usually injected intramuscularly though it may be given by the intravenous route

Dose The initial dose is 1 c cm and the subsequent doses are for adults 4 5 c cm for children 3 c cm and very small children 2 c cm The drug is usually administered on consecutive days for 10 days and then after a rest of ten days the course of ten injections is repeated The immediate cure rate is 95 per cent but the relapse rate is high being about 10 15 per cent

Advantages The drug is well tolerated by the intramuscular route and being least toxic is suitable for treatment of cases with complication e g jaundice ascites renal damage

METHYL GLUCAMINE ANTIMONIATE (*Protostib Glucantime*) It is a pentavalent antimony compound containing 28 35 per cent of antimony and is supplied as a stable 30 per cent aqueous solution.

Mode of administration It is administered by intramuscular injections

Dose The initial dose for adults is 5 c cm and this is increased to the maximum of 15 c cm The drug is best administered on alternate

days till a total of 15 injections has been given In children the initial dose is 2 5 c cm and the maximum dose 5 10 c cm according to age

Advantages It is well tolerated by the intramuscular route and is relatively non toxic The relapse rate is comparable to the best of the pentavalent antimonials *viz* urea stibamine neostibosan etc

AROMATIC DIAMIDINES STILBAMIDINE *(4 4 diamidino stilbene di (β hydroxyethan sulphonate)* It is a non antimonial preparation available in ampoules of 0 15 g each

Mode of administration A freshly prepared one per cent solution in sterile distilled water is used for daily intravenous injections and 10 per cent solution for intramuscular injection The intramuscular injections are very painful though equally effective

Dose The maximum dose is 3 mg per kilogram body weight but ¼ ½ and ¾ of the *maximum dose should be administered in the* first second and third injections This precaution is not necessary for the intramuscular route The injections are given daily

The intravenous injections should be given very slowly for all diamidine compounds A course of 10 12 daily injections is necessary *for ordinary cases 15 injections in resistant cases* A second course is rarely required except in a few case

Advantages 1 In ordinary cases of kala azar the immediate cure rate is about 98 per cent The relapse rate is about 3 to 4 per cent

2 In antimony resistant cases the results of treatment with this drug are satisfactory

Disadvantages 1 Toxic reactions mild or severe occur in 79 per cent cases 2 Treatment with this drug is not successful in cases of post kala azar dermal leishmaniasis or oriental sore

Toxic effects 1 Mild reactions—headache flushing of the face *and burning sensation all over the body*

2 Severe reactions may occur when the drug is administered at a rapid rate intravenously These are transient dyspnœa epigastric pain vomiting diarrhœa palpitation sweating collapse and convulsive twitchings associated with a transient fall of bloodpressure This reaction may be avoided by injecting the drug at a very slow rate or by a hypodermic injection of ½ c cm of adrenaline a few minutes before the injection of the drug

3 *Neurological sequel Most case treated with stilbamidine* develop a troublesome neurological sequel The symptoms are paræsthesia and dissociated anæsthesia with loss of sensation to light

touch and preservation of the pain and pressure sense mainly over the area of distribution of the trigeminal nerve

PENTAMIDINE ISETHIONATE For intravenous injection 1 per cent solution in sterile distilled water is used for intramuscular injection 10 per cent solution is used

Mode of administration Injections are given intramuscularly or intravenously

Dose Maximum dose is 3 to 4 mg per kilogram body weight for all age groups For intravenous injection the maximum dose is reached in two to three stages For intramuscular injection maximum dose may be given from the very beginning

Injections are given daily or on alternate days till a total of 10 injections Following a period of rest for 10 days another course of 10 injections is given

Advantages 1 It is better tolerated and less toxic than stilbamidine 2 There is no danger of diamidino stilbene neuropathy 3 Cure rate is 94 per cent 4 Can be used intramuscularly

Disadvantages 1 Relapse rate is about 15 per cent

2 Occasional case may develop toxic diabete

3 The muscle into which many injections of pentamidine have been given may undergo fibrosis

HYDROXYSTILBAMIDINE ISETHIONATE 10 per cent solution in 2 per cent procaine is used for intramuscular injection and each dose is dissolved in 25 c cm of 25 per cent glucose for intravenous injection This appears to be the best of all the aromatic diamidine The mode of administration is similar to pentamidine but the injection are given on alternate days or on two consecutive days followed by one day s interval Two courses of 10 injections each at an interval of 10-15 days are given for ordinary cases and two courses of 15 injection each for resistant cases The cure rate is 98 per cent and only 4 to 5 per cent relapse occurs It is well tolerated and no neuropathic sequel occurs

RESPONSE TO SPECIFIC TREATMENT In uncomplicated cases of kala azar the response is noticed within a short time The fever usually subsides within about a week of commencement of treatment and there is rapid improvement of general health and gain in weight In cases with oedema there is an initial loss of weight and this is followed by steady gain in weight Three weeks after completion of treatment the spleen shows a marked degree of reduction in size A spleen measuring 4 below the costal margin usually recedes completely or is just palpable while a massively enlarged spleen usually shrinks to less

than half its initial size. The leucocyte count returns to normal and the hæmoglobin value improves to near normal levels.

CRITERIA OF CLINICAL RECOVERY. 1. Subsidence of fever and maintenance of apyrexia. 2. Improvement of general health and significant gain in weight. 3. Considerable decrease of splenic enlargement. 4. Well marked improvement of anæmia.

The only criterion of permanent cure that holds good for 95 per cent of cases is the freedom of the patient from symptoms of kala azar for a period of six months after an apparent clinical cure.

SYMPTOMATIC TREATMENT

Now a days no other treatment excepting the specific one is needed in an average uncomplicated case. But whenever serious symptoms or complications arise they require immediate appropriate treatment.

TREATMENT OF COMPLICATIONS

1. DYSENTERY. (*a*) *Amœbic*—A full course of amœbicidal treatment should be given.

(*b*) *Bacillary*—appropriate treatment should be adopted.

2. ANÆMIA. When anæmia is marked hæmatinics should be given. In severely anæmic patients blood transfusion is indicated.

3. CO-EXISTENT MALARIAL INFECTION. Adequate anti-malarial treatment is also required when malaria becomes overt.

4. HOOKWORM INFESTATION. It should receive appropriate treatment after the completion of the specific antimony treatment.

5. PNEUMONIA OR BRONCHO-PNEUMONIA. Penicillin in the dosage of 500,000 units twice daily is the drug of choice. Broad spectrum antibiotics may be used if penicillin proves ineffective.

6. KALA AZAR COMPLICATED BY TUBERCULOSIS. In view of fatal flare up of pulmonary tuberculosis by antimony therapy the drug of choice in such cases is stilbamidine or hydroxystilbamidine. The patient is treated with strict bed rest and with high caloric diet supplemented with vitamins, hæmatinics and anti-tuberculous drugs. The pulmonary lesions are never adversely affected with stilbamidine or other diamidines and the cure of kala azar definitely improves the chances of cure of pulmonary lesions. For abdominal or glandular tuberculosis aromatic diamidines should be combined with anti-tuberculous drugs. Surgical treatment of tuberculosis is best postponed till kala azar is cured.

7 Agranulocytosis The treatment that has been found useful so far consists of penicillin to combat and prevent secondary infection liver extract or folic acid in large doses in an attempt to raise the leucocyte count measures to prevent peripheral circulatory failure e.g. DOCA diffusible stimulants calcium vitamin C and glucose intravenously and blood transfusion Diet should be light and if necessary partially predigested (e g peptonised milk) to prevent diarrhœa and diarrhœa if present should be treated with tetracyclines In previously untreated cases specific treatment of kala azar with sodium stibogluconate should be adopted In the cases where the complication develops during specific treatment of kala azar a different non toxic compound should be carefully administered a the condition shows improvement

8 Cancrum Oris This condition which is not so much due to the leishmanial infection as to the associated marked leucopenia and anæmia requires immediate specific treatment and energetic treatment for the local condition and the anæmia

Treatment consists essentially of (i) penicillin therapy parenterally in the dosage of 500 000 units twice or thrice daily for 7 to 10 days (ii) daily injections of pentavalent antimonial (iii) high protein diet with hæmatinics and vitamins In cases not responding to specific treatment given along with penicillin and hæmatinics blood transfusion is useful by correcting the anæmia raising the defensive powers of the body and promoting healing of the ulcer

9 Hæmorrhages Slight epistaxis gum bleeding or mild subcutaneous petechial hæmorrhages do not demand any special treatment Oral or parenteral administration of calcium and vitamins C and K with necessary local treatment will usually control the hæmorrhage Specific treatment should preferably be given every other day

Severe hæmorrhages not responding to the above treatment will require blood transfusion Specific treatment with pentavalent antimony should be given with caution preferably in smaller dosage with an interval of 2 to 3 days between the injection

10 Jaundice It is a very unfavourable complication The drug of choice is one of the least toxic antimony compounds like sodium stibogluconate Injections should be given on alternate days or in every cases twice a week If the jaundice persists it is always safer to stop short of the maximum dose The patient should receive minimum of fat in the diet supplemented with moderate amounts

of protein liberal amounts of carbohydrate including glucose and vitamins

RESISTANT CASES AND THEIR TREATMENT

Most cases of kala azar are cured with one or two courses of injections of the specific drugs A proportion of the cases fail to respond satisfactorily to the treatment adopted and another group may have relapse of kala azar usually within six months of apparent clinical cure Such cases are classed as relapsed or resistant cases Use of another anti kala azar drug belonging to the same group but more powerful may result in cure of some of these cases In others the drugs of a group different from the one previously employed prove successful For example a case failing to respond to antimonials may respond to aromatic diamidines and a case relapsing after pentamidine may be cured with pentavalent antimonials A small proportion of cases however prove entirely resistant to drugs These cases usually show evidence of extreme degree of hypersplenism

Previous to the introduction of the aromatic diamidines such cases used to be treated with 3 courses of twelve daily intravenous injections of neostibosan at an interval of twelve days between each course In the first course the initial dose was 0 2 gr subsequent doses were increased by 0 1 g till a maximum daily dose of 0 5 g was reached In the second and third courses the initial dose was 0 3 g In case of little or no improvement after the first course one or two injections of 1 c cm of T C C O (a solution of containing equal parts of turpentine camphor and creosote in two and a half parts of olive oil) used to be given into the gluteal muscle during the second course to stimulate the production of non specific immunity The results were however not very satisfactory

Nowadays stilbamidine is the drug of choice in the treatment of resistant cases where the following lines of treatment should be adopted 15 injections of stilbamidine are given on consecutive days till a total dose of 2 g per 100 lb body weight is reached This is followed by a period of rest for 3 weeks during which period the patient receives supportive treatment with hæmatinics If the patient is not cured clinically a second course of 15 injections is administered In very resistant cases a third course may be necessary Hydroxy stilbamidine in two or three courses may be used It has the advantage of being free from the neuropathic sequel Cases that fail to respond to chemotherapy should be treated with splenectomy followed by 2 3 course of injections of aromatic diamidines

PREVENTIVE MEASURES

The measures for the prevention and control of kala azar are

(*a*) Anti sand fly measures, *i.e.* residual spraying of the dwelling houses, cattle sheds and fowl pens with DDT. For personal prophylaxis, use of fine meshed and fly proof nets at night, spraying of the living rooms with insecticidal solution, and if these are not possible application of and fly repellants like dimethyl phthalate cream to the exposed parts of the body may prove useful.

(*b*) Measures against the reservoir of infection, *i.e.* treatment of all cases of kala azar and post kala azar dermal leishmaniasis and destruction of infected dogs in areas where these are regarded as animal reservoirs should be adopted.

DERMAL LEISHMANOID

[Post kala azar dermal leishmaniasis, Brahmachari's disease]

DEFINITION

Dermal leishmanoid is a chronic granuloma of the skin caused by the protozoan parasite *Leishmania donovani* subsequent to the cure of kala azar. Hypopigmented macules, erythema and nodules are the common types of lesion produced and ulceration is unusual.

ETIOLOGY

Dermal leishmanoid occurs mainly in the old endemic areas of kala azar. In India it has been reported from Bengal, Bihar, Uttar Pradesh, Madras and Assam. A variant of dermal leishmanoid has been reported from the Sudan and East Africa. A small number of cases have been reported from China during recent years. No case of dermal leishmanoid has yet been reported from other kala azar endemic areas of the world, *i.e.* the Mediterranean countries, the U.S.S.R., South America.

The lesions appear in about 5-10 per cent of cases of kala azar after their recovery from the visceral disease. A previous history of kala azar and its specific treatment is obtained in 83 per cent of cases, in 13 per cent of cases history of prolonged fever with splenomegaly that subsided without any injections is obtained; about 4 per cent of cases do not give a previous history suggestive of kala azar.

The interval between the development of dermal leishmanoid and the cure of kala azar is between six months to five years in about 80 per cent of cases.

of protein liberal amounts of carbohydrate including glucose and vitamins

RESISTANT CASES AND THEIR TREATMENT

Most cases of kala azar are cured with one or two courses of injections of the specific drugs A proportion of the cases fail to respond satisfactorily to the treatment adopted and another group may have relapse of kala azar usually within six months of apparent clinical cure Such cases are classed as relapsed or resistant cases Use of another anti kala azar drug belonging to the same group but more powerful may result in cure of some of these cases In others the drugs of a group different from the one previously employed prove successful For example a case failing to respond to antimonials may respond to aromatic diamidines and a case relapsing after pentamidine may be cured *with pentavalent antimonials* A *small proportion of cases however* prove entirely resistant to drugs These cases usually show evidence of extreme degree of hypersplenism

Previous to the introduction of the aromatic diamidines such cases used to be treated with 3 courses of twelve daily intravenous injections of neostibosan at an interval of twelve days between each course In the first course the initial dose was 0 2 gr subsequent doses were increased by 0 1 g till a maximum daily dose of 0 5 g was reached In the second and third courses the initial dose was 0 3 g In case of little or no improvement after the first course one or two injections of 1 c cm of T C C O (a solution of containing equal parts of turpentine camphor and creosote in two and a half parts of olive oil) used to be given into the glutæal muscle during the second course to stimulate the production of non specific immunity The results were however not very satisfactory

Nowadays stilbamidine is the drug of choice in the treatment of resistant cases where the following lines of treatment should be adopted 15 injections of stilbamidine are given on consecutive days till a total dose of 2 g per 100 lb body weight is reached This is followed by a period of rest for 3 weeks during which period the patient receives supportive treatment with hæmatinics If the patient is not cured clinically a second course of 15 injections is administered In very resistant cases a third course may be necessary Hydroxy stilbamidine in two or three courses may be used It has the advantage of being free from the neuropathic sequel Cases that fail to respond to chemotherapy should be treated with splenectomy followed by *2 3 course of injections* of aromatic diamidines

(belt area) the axillæ and the neck often remain unaffected and of normal colour The lesions are not raised above the skin surface (unless nodular lesions develop on these patches) and the loss of pigment is partial and the skin is never ivory white like vitiligo

ERYTHEMA is most commonly seen on the face on the nose the cheek (butter fly erythema) and the chin It may be more generalized and affect the entire body in rare instances The flushed appearance is more prominent after the patient has been out in the sun for sometime

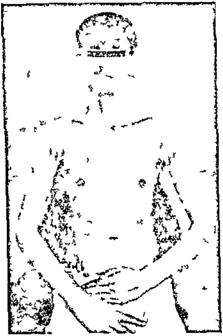


Fig 18 Showing extensive hypopigmented macular and nodular lesions in a case of dermal leishmanoid

NODULES are common ly seen on the chin other parts of the face and less frequently on the ear These may be present in the extremities the trunk and the genitals and produce periony chial induration in occasional cases Nodules may be seen in a small proportion of cases on the mucous surface i e lip tongue inside of the cheek Large tumour like lesions may be produced on the extremities in occasional cases Nodules and other types of lesions of dermal leishmanoid do not ulcerate unless subjected to trauma

In about 75 per cent of the cases of dermal leishmanoid more than one type of lesion is present (Fig 18) This is a useful diagnostic feature

Dermal leishmanoid is usually not associated with the visceral disease kala azar and apart from the cosmetic defect the patient does not suffer from any physical disability like itching irritation or anæsthesia The blood count is usually normal and the aldehyde and the antimony tests negative The complement fixation test for kala azar is positive is about 15 per cent of cases

AGE AND SEX INCIDENCE About 80 per cent of the cases occur in males and about 75 per cent during the second and the third decades of life

CAUSATIVE ORGANISM Dermal leishmanoid is caused by *L donovani*

PATHOLOGY

In the *hypopigmented macular* type of dermal leishmanoid the epidermis shows little change but the pigment in the basal layer is less than that in adjacent normal skin Small islands of cell infiltration consisting of histiocytes lymphocytes and occasional plasma cells are seen in the region of the subpapillary plexus and in relation to the hair follicles sebaceous glands and sweat ducts

In the *erythema* type decrease of pigment is readily seen and the rete cones show some degree of dwarfing There are large collections of histiocytes lymphocytes and plasma cells in the subpapillary region extending often in columns deep into the dermis in the region of the mid dermal venous plexus and around the hair follicles sebaceous glands and sweat ducts Marked dilatation of the vessels in the mid dermal region is seen and there is oedema of the superficial layers of the dermis

In the *nodular* type the epidermis is thin and reduced to a few layers and the rete cones are absent pigment is distinctly diminished A subpapillary clear zone is usually seen and the corium is occupied by a granuloma consisting of histiocytes lymphocytes numerous plasma cell newly formed blood vessels and the cell infiltration is seen in relation to the various structures in the dermis The blood vessels are dilated and some degree of oedema of the superficial layers of the dermis may be present

The parasites are very scanty in hypopigmented macules more readily detectable in erythemas and numerous in nodular lesions They occur inside histiocytes

CLINICAL MANIFESTATIONS

The lesions are essentially of three types *viz* hypopigmented macule erythema and nodule The term nodule has been used to include lesions elevated above the skin surface and of sizes varying from that of small pea to large raised tumours or plaques

HYPOPIGMENTED MACULES or larger patches formed by coalescence of smaller macules occur most commonly on the extensor surfaces of the limbs and lateral parts of the back of the trunk besides the face The lesions may be extensive and affect almost whole of the body but even in such cases the region where the *dhoti* is tied around the waist

5 TUBERCULOID LEPROSY is associated with hypopigmented patches the distribution of which is asymmetrical and commonly on the face buttocks and limbs The condition is associated with sensory disturbance and anaesthesia

B Erythema type of dermal leishmanoid is to be differentiated from the following

1 ACNE ROSACEA is associated with dilated vessels on the nose chin and cheek which appear congested Small red papules develop on follicular openings in this area

2 LUPUS ERYTHEMATOSUS is seen on the cheeks as disc like raised erythematous lesions Similar lesions may appear on the other parts of the body Formation of bullæ and hæmorrhages may be noted

3 DRUG DERMATITIS History of intake of drug

4 LEPROSY is distinguished by the presence of signs of nerve involvement characteristic distribution of the lesions and the presence of the bacillus in smears from lepromatous cases

C Nodular lesions are to be distinguished from acne rosacea and leprosy (*vide supra*)

SPECIFIC TREATMENT

Pentavalent antimony compounds are of value in the treatment of dermal leishmanoid the aromatic diamidines are generally ineffective Treatment with antimonial is contra indicated in cases with tuberculous disease serious hepatic renal or cardiac disease cases of dermal leishmanoid with such complications are best left untreated

Urea stibamine aminostiburea neostibosan solustibosan sodium stibogluconate or methyl glucamine antimoniate may be administered on alternate days till 15 injections have been administered The course of 15 injections is repeated at 2 3 week intervals till 3 4 courses of injections have been given Alternatively urea stibamine group of drugs may be administered twice a week till a total of 50 injections has been given

The erythematous and nodular lesions are the first to be affected by treatment and they show signs of regression after 15 to 20 injections On completion of the full course of treatment majority of cases show complete disappearance of the nodular and erythematous lesions In others a few nodules may persist Hypopigmented macular lesions show marked improvement in about half the cases If the cases are kept under observation further improvement is observed during the next 3 6 months Usually about two thirds of the nodular and erythematous

DIAGNOSIS

CLINICAL DATA 1 History of kala-azar and its specific treatment or of prolonged fever with splenomegaly 6 months to 5 years previous to the development of the skin lesions 2 Character and distribution of the skin lesions and presence of more than one type of skin lesions in an individual case

LABORATORY DATA *Demonstration of the Parasite* A small and soft nodule is snipped off with fine scissors and the cut surface of the nodule rubbed on a few slides to make smears that are stained with a Romanowsky stain and examined for leishmania Smears may also be made by slit and scrape method from larger nodules as in cases of leprosy L D bodies are found inside the histiocytes or more frequently extracellularly due to the rupture of the host cell It is not usually possible to demonstrate leishmania in smears from hypopigmented and erythematous types of lesions But examination of histological sections from any type of lesions of dermal leishmanoid stained with the Feulgen reaction is of value in demonstration of the parasite Also *Leishmania donovani* may be obtained on culture in N N N medium of tissue cells aspirated with strict aseptic precautions from a nodule and washed out with a little citrated saline into the medium A rich growth of leptomonads may be obtained in 7 10 days

DIFFERENTIAL DIAGNOSIS

A Hypopigmented macular type of lesions of dermal leishmanoid are to be differentiated from the following

1 LEUCODERMA is distinguished by the ivory white depigmentation and distribution of the lesions is unlike that of dermal leishmanoid

2 TINEA VERSICOLOR usually affects the face neck central part of the back and front of the chest and the lesions are scaly the fungus is demonstrable on examination of scrapings

3 SEBORRHŒIC DERMATITIS usually affects the scalp the face (eye brows nasolabial folds chin mastoid regions) flexor surfaces and over the sternum or in the interscapular area and the lesions are scaly

4 PITYRIASIS ROSEA is associated with a general eruption of rounded or oval outline often coming on suddenly after slight febrile attack and there is often a herald patch on the trunk appearing several days before the general eruption Face neck and scalp are very infrequently affected and the lesions are seen on the trunk and limbs

certain Arab countries etc sand fly feeding on the margin of a sore and ingesting the leishmania containing histiocytes with its blood meal In about a week or ten days there is heavy growth of flagellates in the midgut and more anteriorly The leptomonads are inoculated into the skin wound made by the sand fly during its feed on man As in kala azar a local focus of infection results but unlike the visceral disease the process remains localised The leptomonads develop in the gut of the



FIG 19 Sloughing oriental sore affecting the lip



FIG 20 Showing oriental sores on the forearm and thigh

PATHOLOGY

The lesion is a chronic granuloma which occupies the corium and may extend to the subcutaneous layer The epidermis is thinned out and ulcerated The granuloma consists of histiocytes many of which contain *L. tropica*, lymphocytes plasma cells newly formed capillaries and fibroblasts Giant cells of foreign body type may also be seen Secondary pyogenic infection may follow through ulcerated epidermis and neutrophils may be seen in large number in the superficial parts of the sore

CLINICAL MANIFESTATIONS

There are two distinct types of oriental sore i.e. the *moist* type which ulcerates rapidly and the *dry* type in which the ulceration i

cases and half the cases with hypopigmented macules* are completely cured and marked improvement is noted in about ⅔rds of the remaining cases In about ⅙th of the total cases no or slight improvement is noted Relapse of dermal leishmanoid after improvement is not very rare In such cases further treatment is indicated

SUBSIDIARY TREATMENT

Administration of potassium iodide in large doses during the first course of injections is held to be useful in the treatment of cases with large and firm nodular lesion X ray exposures and administration of steroid hormone are of doubtful value

ORIENTAL SORE

[Cutaneous leishmaniasis Aleppo boil Delhi boil Lahore sore Sart sore etc]

DEFINITION

Oriental sore is a chronic granuloma of the skin and subcutaneous tissues that proceeds to indolent ulceration and is caused by the protozoan parasite *Leishmania tropica*

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION In the Indo Pakistan subcontinent it occurs in western half of India and West Pakistan Oriental sore *occurs endemically in Afghanistan Iran Iraq Asia Minor* Arab countries in Asia sub tropical regions of the U S S R Egypt and the countries along the Mediterranean coast and the tropical areas in *Africa Mediterranean countries in Europe particularly* Greece Italy Sicily and Central and South America

AGE SEX AND RACE INCIDENCE In endemic areas children form *the majority of cases but foreigners of all ages and sexes are equally* susceptible

SEASONAL INCIDENCE In most endemic areas the incidence is *highest from July to October*

CAUSATIVE ORGANISM *Leishmania tropica* is morphologically and culturally indistinguishable from *L donovani* The leishmanial form is *found intracellularly* in the reticulo endothelial histiocytes in the base of ulcer and the *leptomonad form is found in the gut of the* female sand fly (*e g P papatasii*) fed on cases of oriental sore and in culture

MODE OF INFECTION

Oriental sore is transmitted by the bite of the female sand fly belonging to certain species *viz P papatasii* in India *P sergenti* in

estates in Assam and occasionally among undernourished population in Bengal where oriental sore does not occur It starts as a blister and rapidly develops into a large punched out ulcer with more or less circular and indurated margin and covered with slough Fusiformis and Vincent's spirochætes may be demonstrated in smears made from the sore

2 CUTANEOUS TUBERCULOSIS *Lupus vulgaris* occurring on the face is differentiated by prolonged course characteristic histology and response to anti tuberculous drugs

3 YAWS It occurs among aboriginals in areas where generally oriental sore does not occur It has got a characteristic heaped up appearance and on examination treponema may be demonstrated and the Wassermann reaction may be positive

4 PRIMARY SYPHILIS affecting the lips is distinguished by history and presence of *Tr pallidum* in the exudation obtained from the sore

5 LEPROSY Non ulcerated oriental sore is distinguished by the absence of other features of leprosy and absence of *M lepræ*

6 VELDT SORE Microscopic examination usually shows *C diphtheriæ* in veldt sore The sore starts as a blister and is a shallow ulcer

TREATMENT

Secondary infection which is often present should first be eradicated with antibiotics and local antiseptic treatment When the number of sores is not too large the base of each ulcer may be infiltrated with any one of the following (*a*) mepacrine methanesulpho nate (5 per cent solution) (*b*) sodium stibogluconate (100 mg of Sb/c cm) (*c*) berberine sulphate (2 per cent solution) The sores are taken in turn and 1 6 infiltrations made at intervals of 3 4 days Small sores may heal up after a single infiltration and most are cured within 1 2 months

When there are numerous sores or the sore is so situated that local infiltration is not convenient parenteral administration of antimonials should be resorted to Both tri and penta valent antimony compounds are effective Tartar emetic or sodium antimonyl tartrate 2 per cent solution had been used with success by early workers The dosage used was 1 c.cm initially gradually increased to a maximum of 4 5 c cm the injections being given twice or thrice weekly Lithium antimony thiomalate has also been found to be effective

Of the pentavalent antimonials urea stibamine and similar com

delayed The former is seen in desert settlements and rural areas and the latter in urban area

Incubation period is very short 1 6 weeks in the moist type of sore In the dry type it is usually two to six months

The sores always occur on the exposed parts of the body the face (Fig 19) ears extremities (Fig 20) and the trunk if it is kept exposed The sores are usually *multiple though single* oriental sore is not uncommon There is a case on record in which there were over 230 sores scattered all over the body

The initial lesion is a small itchy papule surrounded by erythema General symptoms are usually absent during the onset and course of oriental sore The papule gradually increases in size and forms a nodular lesion covered by an adherent scab which is formed by drying of a serous exudation through the thinned epidermis and there is a dull red zone of inflammation around the sore The sore is more or less circular in outline and has clean cut indurated margin Secondary infection of the sore leads to pus formation under the adherent scab of the ulcer causing purulent discharge

Untreated oriental sore usually heals up spontaneously in about 6 12 months leaving a deep depigmented scar

In recurrent cases a lupoid type of sore may be produced and this persists for several years

Secondary nodules may occasionally form along the lymphatics and the regional lymph nodes may be enlarged Secondary infection of oriental sore with virulent organisms may lead to cellulitis septic lymphangitis lymphadenitis septicaemia etc

DIAGNOSIS

The clinical features of oriental sore are often characteristic enough for a diagnosis to be made in endemic areas and in people hailing from those areas The diagnosis may be confirmed by demonstration of the parasite *L tropica* in smears of tissue obtained from the depth of the cut made at the margin of the ulcer by the slit and scrape method Histological examination of the tissue obtained by biopsy from the sore is also useful in demonstration of the parasite Also culture made in N N N medium of tissue aspirated from the base of the ulcer often yields a heavy growth of flagellates

DIFFERENTIAL DIAGNOSIS

Oriental sore may have to be differentiated from the following

1 NAGA SORE It is seen frequently among labourers in tea

SUBSECTION B HELMINTHIC DISEASES

CHAPTER V

HOOKWORM DISEASE

[Ancylostomiasis Uncinariasis Anaemia of the miners tunnel works etc]

DEFINITION

It is a disease caused by hookworms living in the small intestine and clinically characterised by anaemia oedema debility and prostration

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The hookworm disease exists in almost all parts of the world It is specially prevalent in tropical and subtropical countries as warmth and moisture are necessary for the development of the infective stage of the parasites outside the body It is present in the coal mines of Continental Europe in the tin mines of Cornwall in Africa and America It occurs frequently in Ceylon Burma Malaya and the East Indies Siam South China and Queensland It is very common throughout India In Bengal there is a high percentage of infections (about 80 per cent) but the degree of infection varies a good deal in different individuals and in different localities

AGE AND SEX INCIDENCE All ages are affected Both sexes are susceptible to the disease

CAUSATIVE ORGANISM There are chiefly two forms of the parasite—(1) *Ancylostoma duodenale* and (2) *Necator americanus*

ANCYLOSTOMA DUODENALE *Adult Stage* The male measures about ½ inch and the female which is longer and stouter than the male is about ¾ inch in length They are cylindrical in form and slightly curved The mouth part of the parasite is powerfully armed with four ventrally situated hooklike teeth with which they pierce the mucosa of the bowel The tail of the female worm is pointed and conical while that of the male is expanded into an umbrella like bursa with which it clasps the female The vulva in the female is situated behind the middle point of the body

Ova These are ovoid in shape 60 *microns* in length and 40 *microns* in width and have a thin wall narrowly separated from the central mass by a clear space all round (Fig 21) The central mass is

pounds neostibosan sodium stibogluconate and methyl glucamine antimoniate have all been found effective The dosage is similar to that used for the treatment of kala azar but the drugs urea stibamine neostibosan and methyl glucamine antimoniate are preferably administered on alternate days or twice a week Most cases are cured with 15 20 injections of pentavalent antimonials

Various local applications to the ulcer such as carbon dioxide snow for 5 30 seconds ointments containing tartar emetic 1 2 per cent or cignolin derivatives or nitrate of mercury or calomel etc have their advocates Irradiation with x rays has been reported to be useful in curing the sore in 10 days but we did not find x ray therapy of much value in treatment Treatment by radium zinc ionization diathermy etc has been recommended by different workers Vaccine therapy using a vaccine made from culture of *L tropica* has been reported to be useful But the results of vaccine therapy have not been satisfactory

In cases where there has been considerable loss of tissue skin grafting is necessary to prevent disfiguring scars

PREVENTIVE MEASURES

Anti sand fly measures as described under *kala azar* are of value in prevention of oriental sore

Prophylactic inoculation of live culture of *L tropica* to produce a sore in covered part of the body (after an incubation period of 2 4 months) confers considerable degree of immunity The sore is protected from secondary infection and allowed to heal naturally in about six months Injection of vaccine prepared from dead cultures of *L tropica* has been reported to be of value in prophylaxis of oriental sore

P C Sen Gupta

MODE OF INFECTION

Man is usually infected by the hookworm larvæ during walking on bare feet or working in fæcally contaminated soil. The larvæ pierce the skin of the part of the body they come in contact. The commonest sites of their entry are the soles of the feet, dorsum of the feet and the hands of gardeners and miners where ground itch or water itch develop. According to Looss the larvæ then reach the subcutaneous tissue from where they enter the superficial venules. By these channels they are carried to the right heart and thence to the lungs. Here they escape from the pulmonary vessels into the air vesicles and thence they crawl up along the bronchi and trachea and larynx and pass down into the œsophagus to reach the stomach and the small intestine on the seventh day. In the intestine they attach themselves to the mucosa and grow to maturity. It takes about six to seven weeks before the ova appear in the stools. During the course of their journey the patient may have sore throat and fever.

PATHOLOGY

The hookworms produce their harmful effect on the system chiefly by loss of blood caused by them though some authors believe that they may secrete some toxins. To produce any harmful effect in the host the parasites must be in sufficient number. Many people may show ova of hookworms in their stool but they may be in perfectly good health because the degree of infection is very slight. The number of worms may vary from 10 to 25 in very light infection to several thousands in very heavy infection. But it must be admitted that the severity of symptoms is not always proportionate to the number of worms. It should be remembered that a light infection in co-existence with malaria, kala-azar or dysentery may produce a serious disturbance to the health.

The characteristic pathological lesions which the worms produce are ecchymoses and small erosions in the intestinal mucosa, in the centres of which they are seen attached. There are usually more erosions in the mucous membrane than the number of worms indicating that they shift from one point to another. The body is anæmic and often œdematous but looks fairly well nourished. Heart may be dilated and may show evidences of fatty degeneration. Liver and kidneys also show fatty changes.

BLOOD CHANGES. The infection produces progressive anæmia in moderately or heavily infected persons.

composed of 2, 4 or 8 segments. Even in fresh stool 2 or 4 segments are rarely seen in the tropics where the development is so rapid that in

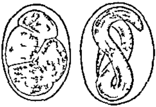


FIG. 21. Ova of hookworm in different stages of development.

stool kept for a few hours the number of segments is 8 or more. Strong sunlight, desiccation and water kill the egg.

NECATOR AMERICANUS. *Adult Stage.* *Necator americanus* closely resembles *A. duodenale* but is somewhat smaller. The mouth has two ventral cutting plates but no teeth. The eggs are similar to those of *A. duodenale*. The head is turned opposite to the general curve of the body. The copulatory bursa is more rounded and its dorsal ray is bipartite instead of being tripartite as in *A. duodenale*. The vulva in the female is situated anterior to the middle of the body.

The adults *of both the types of hookworms inhabit the small* intestine mainly the jejunum and the lower part of duodenum. They attach themselves to the mucous membrane of the bowel by means of their powerful buccal armature. They change the site of attachment *from time to time and the abandoned points continue to ooze blood* for some time. Both these parasites may be found in the same patient. The duration of their lives in the human intestine may be as long as 3-6 years.

The subsequent description in the text is applicable to both types of hookworms.

Larval stage. The development of the embryo in the egg depends *on favourable conditions of moisture and temperature.* Under suitable circumstances an embryo develops in the egg in one or two days after leaving the human host. The embryo known as the *rhabditiform* larva moults twice before it reaches what is called the infective stage *(filariform larva)* which can live for *weeks or months on moist* soil ready to penetrate the skin of any person it comes in contact with

skin is very irritable, inflamed and œdematous and may undergo even sloughing. This local dermatitis is followed 2-4 months later by the development of constitutional symptoms. Mild respiratory symptoms such as cough and gastro-intestinal disturbances, nausea, anorexia, dysentery, diarrhœa may be present at the onset.

In *lightly infected persons* there may not be any symptoms. In *moderately infected persons* there may be lack of energy, loss of appetite, heart burn, acidity, flatulence or other dyspeptic troubles associated with anæmia. In *heavily infected persons* the above symptoms will be exaggerated. There is generally a perversion of taste and appetite and the patient may have a fancy to eat earth, clay (*geophagy*), chalk, hair etc. Abdominal pain, nausea, vomiting, flatulence, constipation or diarrhœa are also present. The pale, puffy face with protuberant abdomen and œdematous feet and legs associated with a comparative sense of well being is a characteristic picture. The patient is markedly anæmic. The skin has a muddy yellow tint. The anæmia may be so pronounced that the patient may look absolutely blanched with marked paleness of the palms, soles, fingers and lips. The tongue is large, pale and flabby. We have seen koilonychia in some cases. There is complete loss of energy accompanied by weakness, prostration, breathlessness with or without exertion, palpitation and hæmic murmurs. In female amenorrhœa is often present. In children there may be retardation of growth both mental and physical. Death may occur from syncope, diarrhœa or asthenia or some intercurrent affection.

COMPLICATIONS

1. Anasarca. 2. Severe anæmia which may rarely be of hyperchromic and macrocytic type. 3. Occurrence of serous effusions into the peritoneal or pleural cavity. 4. Congestive cardiac failure. 5. Secondary pneumococcal or streptococcal infection. 6. Acute diarrhœa or dysentery. 7. Abortion and miscarriage in pregnant women.

PROGNOSIS

The average mortality is low. The prognosis is good if the disease is detected early and promptly treated with specific remedies. But the prognosis in any individual chiefly depends on the following factors:

1. *Age*—Children stand the infection badly. Mental and physical retardation is common.

2. *Intensity of the Infection*—The outlook is worse in severe infection.

Causes of anæmia 1 Loss of blood due to the ingestion of blood by the parasites It has been estimated that each *A duodenale* sucks each day 0 67 c cm of blood and each *N americanus* sucks 0 35 c cm of blood There is also a constant loss of blood by oozing from the points of the bite abandoned by the parasites The reduced coagulability of blood which is produced in this disease is also responsible for further loss of blood by hæmorrhage

2 Deficient intake and utilisation of hæmopoietic factors such as iron and vitamins as a result of digestive disturbances associated with achlorhydria and diarrhœa We think it to be an important factor in the production of anæmia

3 Increased destruction of the red blood cells or a depression of the hæmopoietic function of the bone marrow caused by a hæmolytic toxin secreted by the worms

4 Inflammation of the mucosa and absorption of intestinal toxins through the multiple small wounds produced by the worms causing a depression of the erythroblastic activity of the bone marrow

The anæmia is generally of the hypochromic microcytic type Dimorphic anæmia with macrocytic and hypochromic blood picture (high M C V and low M C H C) has been reported during recent years (*Das Gupta and Chatterjea*) Macrocytosis is due either to deficient absorption of hæmopoietic principle or more probably due to associated deficiency of extrinsic factor The total volume of the blood is increased Coagulation time is prolonged In serious cases with very heavy infection the hæmoglobin may be reduced to as low a figure as 10 per cent (*Helliqe*) It has been estimated that the reduction of hæmoglobin by 1 per cent is brought about by the presence of about 12 worms Poikilocytes and nucleated red cells may be present Another characteristic change is the increase of eosinophil which may go up to 25 per cent or more though the total white cell count is usually normal With the increase of eosinophils there is a proportionate diminution of the neutrophils

CLINICAL MANIFESTATIONS

Signs and symptoms of the disease depend much on the degree and duration of the infection

MODE OF ONSET The onset may occasionally be heralded by the occurrence of a local lesion known as ground or water itch which is a form of dermatitis at the site of entry of the larvæ The lesion consists of a number of vesicle which then turn into pustules with sticky exudate due to secondary pyogenic infection The surrounding

Estimation of the Intensity of Hookworm Infection

It is done by counting the number of ova present in one gramme of fæces according to a special technique (*Stoll's method*). The number of parasites in the bowel may be estimated on the basis of 50 ova in one gramme of stool being equivalent to one parasite. The hookworm load is *light* when the number of eggs per g. of stool is under 2,000; *moderate* if the number is 2,000-10,000; *heavy* if the number is 10,000-40,000; *very heavy* if it is over 40,000 (*i.e.* over 1,000 worms).

DIFFERENTIAL DIAGNOSIS

BRIGHT'S DISEASE (*Subacute diffuse nephritis*). 1. Oedema is not proportionate to degree of anæmia which is often less marked. 2. Blood pressure may be high. 3. Presence of copious albumin and tube casts in urine. 4. High blood cholesterol.

CHRONIC MALARIA. 1. Presence of an enlarged spleen. 2. Icteric tint of the skin and conjunctivæ. 3. History of periodic fever responding to quinine or other antimalarial drugs. 4. Detection of malaria parasites in the blood. 5. Reduction of hæmoglobin in proportion to the loss of red blood corpuscles.

CHRONIC KALA-AZAR. (See under Kala-azar.)

EPIDEMIC DROPSY. 1. History of an epidemic outbreak with incidence of the disease in other members of the family is usually available. 2. Characteristic blotchy cutaneous erythema. 3. Epidemic dropsy nodules are diagnostic. 4. Cardiovascular symptoms are usually present. 5. Glaucoma occurs in 10 per cent. of cases.

BERIBERI (*Wet type with cardiac symptoms*). 1. Acute onset. 2. Anæmia is not so marked. 3. Presence of peripheral nerve involvement. 4. Cardiac symptoms out of proportion to the slight or moderate degree of anæmia.

TROPICAL MACROCYTIC ANÆMIA. High colour index with macrocytosis and megaloblastic bone marrow.

It may be mentioned here in passing that patients suffering from hookworm infection may have malaria or other diseases at the same time.

GENERAL MANAGEMENT

In moderate and severe cases the patient should be confined to bed.

DIET. It should consist of an adequate amount of protein and moderate amount of carbohydrate and fat. It should be sufficiently balanced as regards calories and vitamins.

3 *Degree of Anæmia*—The prognosis is bad in cases with a hæmoglobin percentage below 20 (*Hellige*) and a decrease in the eosinophil count

4 *Presence of Complications*—The co existence of malaria kala azar dysentery and pneumonia renders the prognosis bad

DIAGNOSIS

CLINICAL DATA 1 The characteristic puffy appearance with muddy yellow tint of the skin 2 The character of the tongue 3 Comparative absence of marked distress inspite of the severe anæmia and anasarca

LABORATORY DATA 1 Microscopic examination of the stool showing the presence of hookworm ova 2 Presence of eosinophilia

Techniques for Detection of Hookworm Ova in Stool

(*a*) *Simple smear method* A little fæces is taken on a slide and a very thin emulsion is made with water or normal saline It is covered with a coverslip and examined under the low power of the microscope Each field may show some ova in heavy infection

(*b*) *Concentration methods* In light infections the above method may not be successful in showing the ova and for such cases various methods of concentrating the ova have been advised

(*i*) *Centrifuge method* About one or two grammes of fæces are thoroughly mixed and diluted with water and strained through gauze to remove the large coarse particles It is then centrifuged The centrifuged deposit is now examined under the microscope and if ova be present in the stool the film will show them

(*ii*) *Floatation method* This method is the best and can be very easily carried out as follows

A quantity of the stool about 1 g is thoroughly mixed with saturated solution of common salt in a cylindrical glass container which is filled up to the brim with the fæcal preparation A glass slide is *placed in contact with the surface of the fluid in the container* for twenty minutes The ova float at the top and collect on the under surface of the slide which is then removed and placed under the microscope and examined The method gives positive results in 80 per cent of cases and is better than the smear or centrifuge methods

(*iii*) *Cultural examination* If ova are very scanty hookworm larvæ can be cultured by mixing a quantity of the stools with pure animal charcoal spreading it on the damp filter papers placed in a dish and incubated at 22°C Live larvæ develop within a few days

Precautions 1 The drug must be pure i e free from carbon bisulphide or traces of phosgene 2 Maximum dose should on no account exceed 3 c cm even in strong adults In large doses it damages the liver cells 3 It is better given in one dose 4 It should not be repeated at frequent intervals 5 Patient should not be starved for a long time just before the administration of the drug 6 It should not be given to persons suffering from liver kidney or heart disease and also to weak anæmic and emaciated persons 7 It should be avoided in alcoholics 8 Fats should be withheld from food during administration of the drug 9 Preliminary treatment with oil of chenopodium in case of co existing ascariasis to prevent intestinal obstruction by ascarides

Toxic Symptoms 1 Giddiness and drowsiness 2 Jaundice usually on the 2nd day after the administration of the drug 3 Toxic hepatic necrosis

Oil of Chenopodium It is another very efficient anthelmintic against hookworms The active principle of the oil is *ascaridol* The great disadvantage of the oil is that it contains varying amounts of ascaridol in different samples and so its action is also variable A potent sample should consist at least 70 per cent of ascaridol It is very cheap and so it has been more extensively used Maximum adult dose should not exceed 1 c cm In children upto 16 years the dose is m i for each year of apparent age

Mode of Administration After a light evening meal on the previous day it is best given early in the morning before breakfast in hard gelatin capsules at hourly intervals after a saline purge over night The saline purge (as magnesium sulphate 1 oz) is repeated 2 hours after the last dose to remove the dead or paralysed worms and also the unabsorbed drug Patient should take rest on the day of treatment The treatment may be repeated after 10 days or so if ova persist in the stool One course of treatment removes over 90 per cent of the worms in 80 per cent of cases

Advantage It is effective against roundworms also

Toxic Symptoms 1 Vomiting 2 Headache giddiness and drowsiness 3 Numbness and tingling of the hands and feet 4 Delirium convulsion coma and respiratory failure

Advantages of Carbon Tetrachloride over Oil of Chenopodium

1 No preliminary starvation or purgative is necessary 2 Rest in bed is not necessary except in moderate or severe cases 3 It is cheaper 4 Its taste is less unpleasant and objectionable 5 Its depressant action is less marked 6 Its therapeutic action is better

SPECIFIC TREATMENT

There are several anthelmintic drugs which are very efficient in the treatment of hookworm infection Most of them have more or less toxic effects on the human system and so their administration needs exercise of care and caution

TETRACHLORETHYLENE This is a clear heavy liquid smelling like chloroform It does not mix with water This drug has been found to be very safe and yet effective in the treatment of hookworm infection

Dose The adult dose is 4 c cm For children 4 minims are used for each year of apparent age

Mode of Administration Usually very little preliminary preparation is necessary It is given shaken up with a solution of magnesium sulphate or sodium sulphate Usually one ounce of a saturated solution is used for an adult The treatment is given early in the morning on empty stomach no food except a little hot water is allowed till bowels open When bowels have moved satisfactorily full normal diet is allowed The patient usually experiences a little giddiness sometimes feels sleepy but all these sensations pass off as soon as bowels open Addition of one c cm of oil of chenopodium usually enhances the efficiency of the treatment although the contra indications of the oil of chenopodium should be carefully taken into account before its addition Moreover as patients of hookworm disease are often in poor health the dosage of tetrachlorethylene and oil chenopodium should better be slightly reduced for the sake of safety The treatment may be repeated if necessary after ten days

Owing to the safety cheapness efficiency and simplicity of administration it is the drug of choice for mass treatment

CARBON TETRACHLORIDE It is a heavy colourless liquid It is an effective drug in the treatment of hookworm disease but for it toxicity should not be indiscriminately used in mass treatment It has a stronger action on *N americanus* than on *A duodenale*

Dose 3 c cm is the average dose for an adult and in children 3 minims may be given for each year of apparent age

Mode of Administration Preliminary purge before the administration of this drug is not necessary 3 c cm of the pure drug is given in one dose in the early morning on empty stomach The drug can be given in capsule or preferably in the form of emulsion with 5 to 10 c cm of skimmed milk or with liquid paraffin It should be followed two hours later with a dose of saline purgative The drug should on no account be repeated before 10 days

between the meals for one day only No previous preparation or after purge is needed The drug is non toxic and is given after shaking up with about one and a half ounce of water A do e of 5 g can be used for those above 1 year of age

CASHEW NUT SHELL EXTRACT It is very effective and non toxic This was used in dose of 6 g by the writer and found to be good again t roundworms and other helminths

SYMPTOMATIC TREATMENT

DIARRHŒA Bismuth kaolin

CONSTIPATION Castor oil liquid paraffin etc

FLATULENCE Carminative mixture

INDIGESTION AND LOSS OF APPETITE A mixture containing m 20 30 dilute hydrochloric acid sweetened with a drachm of orange syrup and well diluted with water to be taken after the meal

ANÆMIA *Moderate* Administration of large doses of suitable preparations of iron uch as ferrous sulphate tablets gr 15 18 a day or ferri et ammonii citratis gr 90 120 a day in 3 4 divided doses after meals Dimorphic anæmia with macrocytic hypochromic blood picture must be treated in addition with potent liver extracts or folic acid Liver extract may be given orally as proteolysed liver extract in the dosage of 1 ounce daily for 3 weeks parenterally in the dosage of 4 c cm intramuscularly daily or on alternate days till 10 12 injections are given For parenteral therapy crude liver extract is preferable to refined ones Folic acid is usually given orally in the dosage of 20 30 mg daily for 3 to 4 weeks

S ver Anæmia when severe should always be treated first before specific anthelmintic treatment is instituted In very grave cases of anæmia with a hæmoglobin percentage below 30 blood transfusion may be necessary

HOOKWORM DERMATITIS 1 Antiseptic foot baths

2 Local application of 1 per cent gentian violet solution

3 3 per cent solution of salicylic acid in ethyl alcohol (*Barlo*)

PREVENTIVE MEASURES

GENERAL PROPHYLAXIS 1 Prevention of fæcal contamination of the soil and water in the affected area

2 Adoption of suitable measures for the proper disposal of fæcal matter If pits and trenches are devised they must be at least two feet deep otherwise the larvæ will be able to make their way to

A single treatment will remove 95 100 per cent of the worms especially the Necators 7 It is less dangerous to young sickly children and pregnant women than oil of chenopodium

CARBON TETRACHLORIDE AND OIL OF CHENOPODIUM These two drugs can be given together in the treatment of hookworm disease especially in cases of co-existing round worm infection When combined together and given in adequate and proportionate doses (3 c cm of carbon tetrachloride with 1 c cm of oil of chenopodium) they are more effective but for the sake of safety the dosage of each may better be slightly reduced

Mode of Administration 1 Light diet is given in the previous evening 2 Next morning at 6 or 7 a m one dose of the mixture containing carbon tetrachloride and oil of chenopodium with liquid paraffin upto oz 1 is given 3 One ounce of s s magnesium sulphate is given 2 hours later

In view of the nasty and unpleasant taste of the mixture the drug may be given separately in capsules Carbon tetrachloride is given first and half an hour later the oil of chenopodium This is better than the mixture

HEXYLRESORCINOL It is a white crystalline substance almost insoluble in water It is not so effective as carbon tetrachloride tetrachlorethylene and oil of chenopodium It removes about 70 per cent of the hookworms after two courses of treatment Besides it is costly and entails rigid dietetic restrictions on the previous night

Dose In adults and children over 12 years 5 pill (0 2 g each)

8 12 years	4 pills
6 8 years	3 pills
Below 6 years	2 pills

Mode of Administration The required number of pills is swallowed in one dose without chewing with a glass of water on empty stomach Nothing except water is taken for next 3 hours after which the light meals may be taken Alcohol and fatty foods are avoided A saline purgative may be given 24 hours later to remove the dead worms A second course may be given a fortnight later

Advantages Being almost nontoxic it is suitable for very weak and debilitated patients in whom other drugs are contra indicated

BEPHENIUM HYDROXY NAPHTHOATE (*Alcopar*) has been used with much success This is a yellow insoluble powder with an unpleasant odour

Dose 5 g either in a single dose or repeated three times a day in

CHAPTER VI

ASCARIASIS

DEFINITION

Ascariasis is caused by an infection with the intestinal round worm *Ascaris lumbricoides* and clinically characterised by vague gastro intestinal symptoms and certain reflex symptoms such as nose picking teeth grinding and convulsions

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It has a world wide distribution It is the commonest type of helminthic infection in the tropics

AGE AND SEX INCIDENCE Children are most commonly affected Both the sexes are equally susceptible

CAUSATIVE ORGANISM *Adult Stag* It has a reddish yellow cylindrical body pointed at both ends The male is 6 to 8 inches long with a ventrally curved tail associated with two copulatory spicules The female is much longer 8 to 10 inches in length with a straight tail The mouth of the worm has three lips one dorsal and two ventral The vulva in the female opens ventrally at about the junction of the anterior third with posterior two thirds

The parasite is a common inhabitant of the small intestine especially the jejunum Usually two to six parasites are found but occasionally 800 to 1 000 or even more have been reported

Ova The fertilized ovum is elliptical about 60 *microns* long and 50 *microns* wide has a thick shell surrounded by a brownish yellow or transparent mamillated albuminous envelope (Fig 22) The unfertilised eggs are longer and narrower but may be of other shapes and contain highly refractile granules The eggs are highly resistant to desiccation and to antiseptics such as formalin

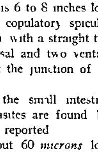


Fig 22 Ovum of *A lumbricoides* (Fertilised)

Infective Stage After passing out of the body of the human host with the fæces the fertilised egg becomes embryonated within 10 to 40 days depending on the atmospheric temperature and humidity

the surface of the soil and they must be filled up with earth and fresh ones made from time to time

3 Educative propaganda to remove the promiscuous habit of the people to defaecate on any and every part of the soil and to infuse better sense of sanitary habits

4 Mass treatment of carriers

PERSONAL PROPHYLAXIS 1 Use of shoes or boots if possible while walking on badly contaminated soil especially in rainy season

2 Common salt which is very cheap has been advocated as a useful measure It is sprinkled over the contaminated soil stools or over the floors of latrine in sufficient quantity It has an injurious effect on the larvae when it comes in contact with them

N V B

REFLEX SYMPTOMS Mental irritability nose picking teeth grinding anal pruritus nocturnal enuresis convulsions strabismus and meningismus are frequently seen as a result of the reflex irritation of the central nervous system

MECHANICAL SYMPTOMS They have already been described under pathology

COMPLICATIONS

1 Intestinal obstruction 2 Intussusception 3 Intestinal perforation and peritonitis 4 Appendicular obstruction 5 Laryngeal obstruction 6 Pneumonia during larval migration 7 Jaundice liver abscess and cholecystitis

PROGNOSIS

The mortality from ascariasis is almost nil But serious complications may ensue as a result of migration of the worms into the various organs and tissues

DIAGNOSIS

In every case of general ill health in children the possibility of ascariasis should be kept in mind The diagnosis should be made on the following data

CLINICAL DATA 1 History of passage of roundworms 2 Presence of suggestive symptoms such as nose picking teeth grinding anal pruritus and convulsions

LABORATORY DATA 1 Blood examination shows moderate eosinophilia 2 Stool examination shows the characteristic elliptical ova with the bile stained albuminous envelope 3 Radiological examination of the gastro intestinal tract with the barium meal may show in some cases the barium filled intestine of the worms

DIFFERENTIAL DIAGNOSIS

Ascariasis may simulate cholecystitis duodenal ulcer intussusception and intestinal obstruction

GENERAL MANAGEMENT

The bowels should be kept open regularly The diet should be adequate in calories vitamins and mineral salts especially iron

SPECIFIC TREATMENT

Santonin and oil of chenopodium are the two potent specific remedies against the worm

MODE OF INFECTION

The embryonated eggs gain entrance to the human host through contaminated food drink or raw vegetables and reach the small *intestine where the embryos are liberated Each embryo penetrates* through the intestinal mucous membrane into the portal blood stream which carries it to the liver and then to the lungs *via* the right side of the heart The subsequent course from the lungs to the small intestine is the same as that of the hookworm larva In the small intestine the larva develops into a mature worm which begins to produce egg about two to three months from the time of infection

PATHOLOGY

The adult worms may cause a chronic intestinal catarrh Their migration may lead to intestinal perforation and peritonitis especially in cases associated with typhoid or amœbic ulceration to appendicular obstruction blockage of the bile duct leading to jaundice pancreatic duct obstruction giving rise to inflammatory changes in the pancreas Intestinal obstruction may be produced by impaction with a large bunch of worms or by intussusception due to the worms Occasionally the worms may pass up the œsophagus and pharynx and then go down the larynx causing respiratory obstruction Benerjea has seen one such case where a child of two years convalescent from diphtheria suddenly developed dyspnœa after he had vomited a roundworm This fact gave the clue The child was caught by the leg and the throat was tickled with a feather till another big roundworm came out of the mouth causing an immediate relief of the dyspnœa

In the stage of larval migration the lungs may occasionally show evidences of pneumonic and bronchopneumonic changes associated with hæmoptysis Urticarial eruptions and rarely nephritis may also occur

CLINICAL MANIFESTATIONS

In many cases there are no symptoms The first evidence of the disease is the passage of the adult worm in the stools or rarely in the vomit When symptoms arise they are usually (*a*) toxic (*b*) reflex or (*c*) mechanical in origin

TOXIC OR ALLERGIC SYMPTOMS These symptoms are probably due to *ascaron* They consist of periodic febrile attacks pallor loss of weight or failure to gain in weight urticarial eruptions conjunctivitis itching of the skin dyspnœa abdominal pain vomiting diarrhœa and dysentery The blood shows a moderate eosinophilia which is however not constant

CASHEW NUT SHELL EXTRACT (Vide Hookworm Disease)

BEPHENIUM HYDROXY NAPHTHOATE may also be used with success (Vide Hookworm Disease)

DITHIAZANINE (3 3 di ethylthiadicarbocyanine iodide) has been used with much success This powder is used as enteric coated tablets The adult dose is 100 to 200 mg thrice daily for 5 days

SYMPTOMATIC TREATMENT

Anorexia anaemia convulsions should receive appropriate treatment Mechanical complications will require surgical interference

PREVENTIVE MEASURES

The preventive measures consist of the following

1 Boiling of drinking water 2 Avoidance of eating raw vegeables 3 Scrupulous observance of personal hygiene 4 Proper disposal of sewage

N V B

SANTONIN *Dose* gr 3 for adults and gr ½ to 1 for children

Mode of Administration After a preliminary purge in the morning the patient is given an early light evening meal At bed time santonin is given along with sodii bicarbonatis followed on the morrow by a saline purge For an adult gr 3 of santonin and gr 10 of sodii bicarbonatis are given together Contrary to the accepted belief santonin may be given dissolved in half an ounce of castor oil without producing any toxic symptoms *(Gunn)*

Toxic Symptoms 1 Epigastric pain 2 Vomiting 3 Headache 4 Delirium and convulsions 5 Dysuria and hæmaturia 6 Xanthuria (yellow urine) 7 Xanthopsia (yellow vision)

OIL OF CHENOPODIUM *Dosage* m 10 15 in adults and m 1 for each year of apparent age in children

Mode of Administration The oil of chenopodium is given in single or repeated doses in capsules or on a lump of sugar or in a mixture with liquid paraffin as in hookworm disease followed by a saline purge 2 hours later Maplestone advocates the administration of gr 3 of powdered santonin with 1 c cm of oil of chenopodium early in the morning before breakfast followed by a saline purgative 2 hours later

HEXYLRESORCINOL It may be given to adults orally in doses of 1 g in capsules in empty stomach A thorough preparation is made by giving a saline purgative on the previous afternoon and putting the patient on milk diet at night Early next morning the drug is given on empty stomach No food except plenty of water is given for the subsequent 3 hours A saline purgative may be preferably given 24 hours later to remove the dead worms A single dose will remove about 95 per cent of the ascarides It is an expensive drug and hence not suitable for mass treatment

If ascaris ova are found on examination of the stools at the end of two weeks a further course of treatment should be repeated

PIPERAZINE Various piperazine derivatives *e g* diethylcarbamazine piperazine diphenylacetate piperazine tartrate have been used either as a large single dose or multiple daily doses for 5 days Either tablets or syrups or elixirs are used

Dose It is expressed as equivalents of piperazine hexahydrate Single dose 2 g of hexahydrate for those of body weight 30 to 50 lb 2 5 g for those between 51 to 100 lb and 3 5 g for those of 101 lb body weight Multiple dose 25 mg of hexahydrate per lb body weight daily in divided doses for 5 days An after purgative may be used when the therapy is completed

symptoms such as nose picking pruritus and insomnia 4 Slight anæmia 5 Occasional eosinophilia of a slight degree

COMPLICATIONS

1 Insomnia and neurasthenia 2 Catarrhal appendicitis 3 Nocturnal enuresis in children 4 Vaginal discharge in young girls

DIAGNOSIS

Eggs are best demonstrated from swabs taken from the perianal skin Stools do not reveal eggs in more than 5 per cent of cases Inspection of the anal region at night immediately after itching begins may show the gravid female worms in the perianal region

GENERAL MANAGEMENT

The bowels should be regularly kept open by the use of grey powder and saline purgatives The diet should consist of restricted amount of sugar

SPECIFIC TREATMENT

The eradication of *Enterobius vermicularis* especially in adults is a difficult problem because of reinfection Measures for prevention of reinfection should be adopted along with any of the drugs used Oil of chenopodium or tetrachlorethylene may be used as anthelmintics after a preliminary saline purge on the previous night Hexylresorcinol in doses of 0 1 g for each year of age upto 10 years and of 1 g for adults in pill form or in capsules by mouth is an efficient remedy The mode of administration of hexylresorcinol is the same as that in hookworm disease Warm retention enemata containing salt water (20 per cent) thymol (1 in 2500) hexylresorcinol (1 in 1000) or infusion of quassia 6 to 8 ounces (1 in 40) are given after a preliminary rectal wash out with 2 per cent sodium bicarbonate solution on the same night and thereafter once a week The rectal administration of drugs is however of doubtful value as it can hardly affect the worms which are chiefly in the cæcum

Medicinal Gentian Violet (*Meroxyl*) Given in enteric coated tablets has been found to be the most efficient remedy against thread worm in about 90 per cent of cases

Dose In adults one gr 1 tablet three times daily one hour before meals for 7 days After a period of rest for 7 days repeat for 7 days

CHAPTER VII

ENTEROBIASIS

[Threadworm disease Oxyuriasis]

DEFINITION

It is caused by infection with the threadworm *Enterobius vermicularis (Oxyuris vermicularis)*

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It has a world wide distribution

AGE Children are especially susceptible

CAUSATIVE ORGANISM *Adult Stage* The adult worm which inhabits the upper part of the large intestine especially the cæcum and also the appendix is thread like in appearance and white in colour The male is 2 5 mm long with a coiled tail The female is 10 mm long and has a long pointed tail

Ova These measure 50 *microns* in length and 25 *microns* in breadth are plano convex and have two shells the outer thick and transparent the inner thin enclosing a coiled embryo (Fig 23)

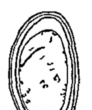


FIG 23 Ovum of *E vermicularis*

MODE OF INFECTION

Infection occurs in man through ingestion of eggs contaminating food water and vegetables The ingested eggs hatch out in the small intestine whence the larvæ after two moults pass into the cæcum where in course of two weeks they develop into mature adults Males fertilize the females and die and are cast out The gravid female worms pass down the rectum and come out of the anus of the human host during sleep at night depositing ova in large numbers at the peri anal region causing pruritus Sometimes they migrate into the female genital tract and urinary bladder The fingers are infected by ova during scratching and are a source of re infection by the mouth and sometimes through the nose

CLINICAL MANIFESTATIONS

Usually the clinical manifestations are none Some authorities believe that the worms may cause the following

1 General ill health 2 Marked constipation 3 Reflex

CHAPTER VIII

TRICHURIASIS

[Trichocephalasis Whipworm disease]

DEFINITION

It is a disease caused by the whipworm *Trichuris trichiura*

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is very common in the tropics though world wide in its distribution

CAUSATIVE ORGANISM *Adult Stage* The male is about 30 40 mm long the female being a little smaller than the male The worm has a very thin anterior and a thick posterior portion thus looking like a whip The posterior end is coiled up into a spiral in the male but almost straight in the female It inhabits the cæcum and large intestine of man



FIG 24 Ovum of *T trichiura*

Ova The ova are brownish in colour and barrel shaped 50 *microns* in length and 25 *microns* in diameter with a clear knob like projection at each end (Fig 24)

MODE OF INFECTION

Infection occurs in man by direct ingestion of embryonated eggs through contaminated food and drink In the small intestine the eggs liberate the larvæ which reach the large intestine and develop into the adult worms within a month

PATHOLOGY

The worms may produce ulceration in the cæcum colon appendix and lower ileum and give rise to secondary infections

CLINICAL MANIFESTATIONS

There are no distinctive clinical features apart from slight anæmia occasional urticaria and eosinophilia in light infections In heavy infections dysenteric symptoms are produced

DIAGNOSIS

It is made by detection of characteristic ova in the stool

Below 16 years gr 1/6 for each year of age daily in divided doses for 8 days After a rest period of one week another course for 8 days may be repeated

Toxic effects None in most of the cases In a few instances nausea vomiting abdominal pain and diarrhœa have been found

Contraindications In severe cardiorenal and hepatic disease alcoholism and ascariasis where there is risk of causing intestinal obstruction due to clumping of round worms it is contraindicated

DIPHENAN (*phenylcarbonate diurate*) It acts directly on the worms killing them in 5 minutes For adults the dose is 1 g thrice daily before meals for one week The dose for children is proportionate to age

Phenothiazine a tasteless thiazine dye is claimed to be very effective but the drug is toxic

PIPERAZINE DERIVATIVES Recently piperazine preparations have been found useful Usually these contain piperazine hydrate and are available in the form of syrups or elixirs These drugs are used for a period of 7 to 10 days in the same dosage as in ascariasis Single dose therapy is of no value

SYMPTOMATIC TREATMENT

ANAL PRURITUS 1 Wearing of gloves in the hands

2 Application of carbolised paraffin or dilute ammoniated mercurial ointment 10 gr to 1 oz which also kills the eggs

PREVENTIVE MEASURES

The secret of successful treatment is the prevention of auto infection

1 Wearing of a night dress to prevent re infection by scratching the perianal region

2 Wearing of gloves or splinting the elbows for the same purpose.

3 Careful washing of hands and cleaning of finger nails after defæcation

4 Smearing the anal region at bed time with the mercury ointment

5 Use of separate bed by the infected children

6 Periodic boiling of the clothes

N V B

CHAPTER IX

TRICHINIASIS

[Trichinosis Trichinellasis]

DEFINITION

It is a disease caused by infection with the embryos of *Trichinella spiralis* and clinically characterised by acute gastro intestinal symptoms during the period of invasion and by fever muscular aches and pains dysphagia and even dyspnœa during the stage of migration

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It is common in Europe and U S A where raw or insufficiently cooked ham is taken Several outbreaks have been recently reported from England It is also found in Africa Syria and China

AGE AND SEX INCIDENCE No age is immune Both sexes are equally susceptible

CAUSATIVE ORGANISM *Adult Stage* The parasite is cylindrical with a pointed anterior end The male is 1 5 mm long with two copulatory spicules at the posterior end The female is about twice the length of the male and is ovo viviparous The worm is usually an inhabitant of the small intestine of pig and sometimes rat where the female liberates the embryos which migrate into the muscles and encyst

Larval Stage The larva consists of a coiled worm with a thin pointed anterior end and thick rounded posterior end enclosed in an oval laminated capsule embedded in the muscle tissues of the pig and sometimes rat

MODE OF INFECTION

The encysted larval trichinellæ gain access to the small intestine of man through ingestion of raw or imperfectly cooked trichinous pork and larvæ are liberated as a result of the solvent action of the gastric juice on the capsule The larvæ rapidly grow into mature adult worms The gravid females penetrate through the intestinal mucous membrane into the submucous layer and begin to give off a large number of embryos which enter the systemic circulation *via* the portal blood stream liver right heart lung and left heart and settle down in the various muscles within two to six weeks of the ingestion of infected meat

TREATMENT

Administration of thymol and oil of chenopodium in appropriate doses may be helpful The combined treatment with tetrachlorethylene and oil of chenopodium is also somewhat effective (*Maplestone*) Faust advocates the use of hexylresorcinol The anthelmintic action of these drugs is enhanced by a preliminary saline purge and high alkaline enema The eradication of the infection is however very difficult Recently dithiazanine has been found to be very effective The dosage used is 100 to 200 mg three times a day for 1 to 3 weeks

N V B

COMPLICATIONS

1 Pulmonary complications such as pneumonia pleurisy and hæmoptysis 2 Neurological complications such as focal pareses with signs of meningitis or encephalitis The cerebrospinal fluid may be normal or may show an increase of cells and protein and occasionally presence of motile trichinella larvæ 3 Neuro retinitis 4 Paralysis of the muscles of respiration 5 Typhoid state in severe infections with myocarditis

SEQUELÆ

Complete recovery is the rule though the following sequelæ may occur 1 Anæmia 2 Thrombo phlebitis 3 Muscular pain or stiffness persisting for a few months 4 Permanent paralysis—rarely

PROGNOSIS

It is influenced by the severity of the infection The mortality rate varies from 1 to 30 per cent Death occurs on the 5th to 7th week from severe toxæmia myocarditis pneumonia encephalitis or diaphragmatic paralysis

DIAGNOSIS

The diagnosis is based on the following data

CLINICAL DATA 1 History of ingestion of infected pork 2 Presence of acute gastro intestinal symptoms 3 Oedema of the face and eyelids with moderate fever 4 Respiratory symptoms such as cough and pain in the chest 5 Urticarial eruptions 6 Sub ungual splinter hæmorrhages

LABORATORY DATA 1 Leucocytosis with high eosinophilia

2 Detection of larval trichinellæ on microscopic examination of the sediment obtained by centrifuging 5 10 c cm of blood laked by 3 per cent acetic acid solution during the stage of migration within the first three weeks often difficult

3 Detection of the encysted larvæ after the third week of the illness by biopsy of a piece of the affected voluntary muscles such as the deltoid or gastrocnemius

4 Detection of the parasites (adults or even embryos in the later stage) on examination of the stools often difficult

5 Positive intradermal test and precipitin reaction with trichinella antigen after the third week

6 Demonstration of the calcified cysts on x ray examination of the affected muscles six months after infection The cysts are however too small to be detected radiologically during life

PATHOLOGY

During migration the larvæ may be detected in the peripheral blood between the 7th to 15th day On reaching the muscles the larvæ lose their motility and become encapsulated in fibrous tissue and later calcified The encysted larvæ may live as long as 20 to 25 years The muscles commonly involved are the jaw muscles the deltoids biceps intercostals diaphragm and gastrocnemius

CLINICAL MANIFESTATIONS

The clinical features are extremely variable The onset may be insidious with a few or no symptoms depending on the degree of parasitic infection and the resistance of the host In a typical case the following stages are often present

STAGE OF INVASION Within a week of ingestion of the infected pork acute gastro intestinal symptoms such as loss of appetite epigastric pain vomiting diarrhœa occasionally accompanied by the passage of blood and mucus appear

STAGE OF LARVAL MIGRATION This stage is characterised by the appearance of the following symptoms within 7 to 14 days of the infection

1 Remittent fever 102° 104°F with low bloodpressure and erythema of face may be present 2 Oedema of the face and eyelids with chemosis of the conjunctivæ appearing as early as the 7th day 3 Oedema of the extremities with pain and tenderness of the under lying muscles may be present 4 Cough and chest pain are often present 5 Splenic enlargement is not uncommon Enlargement of the lymph nodes rare 6 Hard painful small lumps in such muscles as the jaw muscles biceps deltoids intercostals gastrocnemii 7 Dysphagia dysarthria and dyspnœa due to myositis of the tongue laryngeal intercostal and diaphragmatic muscles respectively 8 Skin eruptions urticarial morbilliform and nodular—not common 9 Subungual splinter hæmorrhages especially in 60 70 per cent severe cases almost pathognomonic (*McNaught*) 10 Increased white cell count of 15 000 30 000 per c mm with an eosinophilia of 50 70 per cent occurring in two waves The peak of the primary wave occurs about the third week of the illness and that of the secondary wave at the eleventh week.

STAGE OF ENCYSTMENT The above symptoms continue but complications are likely to occur

CHAPTER X

TÆNIASIS

[Tapeworm Disease]

DEFINITION

Tæniasis is caused by infection with a tapeworm and clinically characterised sometimes by gastro intestinal disturbances varying degrees of anæmia and nervous symptoms

ETIOLOGY

There are five important varieties of tapeworms i (*a*) *Tænia solium* the pork tapeworm (*b*) *Tænia saginata* the beef tapeworm (*c*) *Hymenolepis nana* the dwarf tapeworm (*d*) *Echinococcus granulosus* and (*e*) *Diphyllobothrium latum*

Tænia solium

GEOGRAPHICAL DISTRIBUTION It is prevalent wherever pork is eaten by the people Hence it is common in Germany France and Great Britain but definitely rare in India where most people do not take pork

AGE AND SEX INCIDENCE No age is immune Both sexes are equally susceptible

CAUSATIVE ORGANISM *Adult Stage* It is 2 7 metres long and has a small pin sized head (*scolex*) with four suckers and a rostellum with two row of hooklets The body consists of eight to nine hundred segments (*proglottides*) the largest and gravid ones being farthest from the head The uterus which is situated in the centre of the gravid segments has 7 12 lateral branches on each side of the central uterine stem The eggs are globular 30-42 *microns* in diameter have a thin outer shell and a thick brownish radially striat d envelope (Fig 25) enclosing an embryo with six hooklets called the *onchosph re*



FIG 25 Ovum of *T solium* without outer shell

Larval Stage (*Cysticercus cellulosæ*) The segments containing the eggs are passed out of the intestine singly or more commonly in groups of 4 to 6 with the fæces of the human patient (*the d finit e host*) ingested by the pig (*the int rmediate host*) and reach its intes

DIFFERENTIAL DIAGNOSIS

The disease has to be differentiated from the following

1 TYPHOID FEVER (See page 65)

2 INFLUENZA (See page 65)

3 PNEUMONIA (See page 65)

4 BACTERIAL FOOD POISONING (See under Cholera)

5 CHOLERA (See page 65)

6 ACUTE BACILLARY DYSENTERY (See page 66)

7 RHEUMATIC FEVER (i) Presence of wandering polyarthritis (ii) Evidence of carditis (iii) Very high E S R

8 ACUTE OR SUBACUTE DIFFUSE NEPHRITIS Presence of albumin and casts in the urine

GENERAL MANAGEMENT

Nutrition should be maintained by an adequate diet and during convalescence massage and hot baths are helpful in relieving the muscular stiffness

SPECIFIC TREATMENT

There is no specific remedy Efforts are made to expel the adult worms by administration of calomel followed by saline purgatives Anthelmintics such as santonin thymol Filix mas and turpentine have been used but without any beneficial results It is probable that the oral use of phenothiazine in the adult dose of 8 g daily for 7 10 days may reduce the severity of the trichina infection in man as it has done successfully in 75 per cent cases of experimental trichiniasis in rats (*McNaught*)

SYMPTOMATIC TREATMENT

MUSCULAR PAINS 1 Hot application of antiphlogistine 2 Use of opium preparations

PREVENTIVE MEASURES

Preventive measures consist of 1 Avoidance of eating raw or imperfectly cooked ham 2 Inspection of meat at the slaughter house 3 Rat destruction to prevent infection of the pigs 4 The viscera and carcasses of pigs dying of the disease should be properly disposed of 5 Offals of pigs should not be used for feeding the pigs

N V B

CHAPTEP X

TÆNIASIS

[Tapeworm di ea e]

DEFINITION

Tænia is is cau ed by infection with a tapeworm and clinically characterised sometimes by ga tro intestinal disturbances varying degrees of anæmia and nervous symptoms

ETIOLOGY

There are five important varieties of tapeworms vi (a) *Tænia solium* the pork tapeworm (b) *Tænia saginata* the beef tapeworm (c) *Hymenolepis nana* the dwarf tapeworm (d) *Echinococcus granulosus* and ( ) *Diphyllobothrium latum*

Tænia solium

GEOGRAPHICAL DISTRIBUTION It is prevalent wherever pork i eaten by the people Hence it is common in Germany France and Great Britain but definitely rare in India where most people do not take pork.

AGE AND SEX INCIDENCE No age is immune Both sexes are equally susceptible

CAUSATIVE ORGANISM *Adult Stage* It is 2 7 metres long and has a small pin sized head (*scolex*) with four suckers and a rostellum with two rows of hooklet The body consists of eight to nine hundred segments (*proglottides*) the largest and gravid ones being farthest from the head The uterus which is situated in the centre of the gravid segments has 7 12 lateral branches on each side of the central uterine stem The eggs are globular 30 42 *microns* in diameter have a thin outer shell and a thick brownish radially striated envelope (Fig 25) enclosing an embryo with six hooklets called the *onchosph re*



FIG 25 Ovum of *T solium* without outer shell

Larval Stage (*Cysticercus cellulosæ*) The segments containing the eggs are passed out of the intestine singly or more commonly in groups of 4 to 6 with the fæces of the human patient (*the d finiti host*) ingested by the pig (*the int rmediate host*) and reach its intes

time where the shell is dissolved and the liberated embryo bores its way by means of the hooklets through the intestinal mucous membrane into the lymph or the venous stream It is carried by circulation and finally settles down usually in the muscles of the pig especially those of mastication the tongue shoulders neck and diaphragm loses its hooklets and transforms itself into a cyst (*the cysticercus stag*) The pork infected with such cysticerci is called measly pork This stage may *occasionally occur also in man as a result of auto-infection or exogen*ous infection through ingestion of ova of *T solium* with food or drink The cysticerci may be found in the skin subcutaneous tissues muscles rarely the lungs liver eyes and the brain

MODE OF INFECTION

When uncooked or insufficiently cooked pork infected with cysticercus is ingested by man the cyst wall is digested and the scolex which is evaginated and attaches itself by means of the suckers and hooklets to the mucous membrane of the duodenum or upper jejunum and goes on producing by a process of budding segments which together with the head form the adult tapeworm until after a period of about 3 months gravid segments begin to pass out with the fæces

CLINICAL MANIFESTATIONS

INTESTINAL TÆNIASIS The patient may not complain of any symptoms When present they may consist of anorexia voracious or capricious appetite vomiting vague abdominal pains diarrhœa In adults a state of neurasthenia is sometimes present as a result of the passage of segments in their stools In children itching of the nose and anus convulsions headache and strabismus may be present Blood examination may show various grades of anæmia and often shows an increase of the eosinophils

SOMATIC TÆNIASIS (*Cysticercosis*) Complains of muscular weakness and muscular cramps may be present Small nodules sometimes painful varying from the size of a pea to that of a walnut may be felt under the skin

In cases of involvement of the brain which is not uncommon especially in British soldiers who have served abroad as pointed out by MacArthur the symptoms consist of epileptic fits tremors muscular weakness and mental disturbances which may lead to an erroneous diagnosis of disseminated sclerosis encephalitis cerebral tumour and delusional insanity

DIAGNOSIS

The diagnosis is based on the following data

INTESTINAL TÆNIASIS 1 Presence of segments showing 7-12 lateral branches on each side of the central stem of the uterus 2 Presence of the spherical thick shelled ova containing the embryo with six hooklets

CYSTICERCOSIS 1 Presence of eosinophilia—not a constant finding 2 Microscopical examination of an excised subcutaneous nodule 3 Presence of calcified nodules in the muscles of the limbs or in the brain on x ray examination in cases of infestation of more than 4 years duration 4 Presence of retinal lesions 5 Positive intra dermal and complement fixation tests 6 Positive precipitin test

SPECIFIC TREATMENT

The drugs used for intestinal tænia is are mepacrine hydrochloride Filix mas extract containing 6 per cent filicic acid carbon tetrachloride tetrachlorethylene the first mentioned one being the best

The patient must first be thoroughly prepared preferably for two days A saline purgative is first given and the residue free light diet consisting of milk barley water tea glucose fruit juice etc is allowed On the evening previous to the day of specific therapy a purgative is again used and liquid diet is allowed for the night The specific drug is used the next morning

MEPACRINE HYDROCHLORIDE The patient is put to bed and early in the morning is given a sedative *e g* phenobarbitone gr ii for adults Half an hour later mepacrine hydrochloride is used two tablets 0 1 g each every 10 minutes till a total of 8 to 10 tablets are given A small amount of sodium bicarbonate is given each time with the tablets which are swallowed with a small amount of water Two hours after the last dose of tablets is given a saline purgative is used Normal diet is allowed after bowels move freely The stools passed are all collected and searched for the head of the tapeworm by careful sieving If the head is not found one should wait for three months when the segments will appear in the stool If the head of the tapeworm is not expelled the therapy may then be repeated As mepacrine sometimes causes cerebral excitement and psychosis cases to be treated should be carefully chosen and patients with history of psychological disturbances should rather not be given this drug

The whole amount of the drug suspended in water may be given by a duodenal tube Bhaduri obtained a cure rate of 90 per cent

FILIX MAS *Dose* Maximum adult dose of *Extractum filicis liquidum* is 90 minims (6 c cm)

Mode of Administration After preparing the patient for 2 days the fresh ethereal extract of Filix mas is given on the morning of the third day on empty stomach at half hourly intervals in 3 divided doses in gelatin capsules or in emulsion to hide the nauseating taste and prevent vomiting A saline purgative such as one ounce of magnesium or sodium sulphate is administered one hour after the last dose of Filix mas Castor oil should not be used as a purgative as it causes an absorption of the drug and produces toxic symptoms in 57 per cent of cases No food should be given till bowels have been emptied by the purgative It is necessary to wait for about three months till segment reappear in the stool when the treatment is repeated In resistant cases the treatment may have to be repeated 4 to 5 time

The following method is advocated by D Antoni to be more effective After a preliminary purge the following mixture is given by duodenal intubation—oleoresin of male fern dr i saturated solution of sodium sulphate oz i mucilage acacia dr ii and water oz ii No further medication is required and the whole worm is expelled within one hour

Toxic Symptoms (*a*) Headache (*b*) Giddiness (*c*) Slight jaundice (*d*) Gastro intestinal disturbances *e g* abdominal pain vomiting diarrhœa (*e*) Dyspnœa and cyanosis (*f*) Albuminuria hæmaturia rarely (*g*) Dimness of vision yellow vision occasionally optic neuritis (*h*) Delirium coma and convulsion rarely in severe cases

Contraindications 1 Marked debility 2 Myocardial weakness 3 Severe anæmia 4 Cirrhotic or fatty liver 5 *Nephritis* 6 Pregnancy

CARBON TETRACHLORIDE *Dose* Maximum adult dose i 3 c cm (45 minims) Dose in children is 1 5 c cm

Mode of Administration Prolonged starvation is avoided The patient is put on light diet consisting of barley water fruit juices glucose on the night previous to the day of treatment On the following morning the appropriate dose of pure carbon tetrachloride is given at one dose in an ounce of skimmed milk or preferably emulsified in two ounces of saturated solution of magnesium sulphate Alcohol is forbidden for 2 3 days before and after treatment

Advantages 1 It is more effective than Filix mas Mukerji

and Maplestone obtained a good cure rate 2 It is cheaper 3 It may be administered to ambulant patients

Common Toxic Effects 1 Epigastric discomfort and pain 2 Nausea 3 Headache and giddiness 4 Transient drowsiness

Rare Toxic Effects 1 Jaundice 2 Pain in the lumbar region hæmaturia albuminuria 3 Collapse and coma

Contraindications They are the same as those of Filix mas

TETRACHLORETHYLENE *Dose* 4 c cm for adult

Mode of Administration The patient is prepared as before 3-4 c cm of the drug is mixed with two ounces of saturated solution of sodium sulphate shaken up vigorously and administered immediately on empty stomach early in the morning A light meal is given only after the bowels have moved freely

The drug is safer but less effective than carbon tetrachloride Mukerji and Maplestone obtained a cure rate of 54 per cent

For somatic tæniasis (cysticercosis) the following are advocated 1 Surgical removal of accessible cysts if they are not multiple 2 Treatment of symptoms such as fit by luminal and bromides mesantoin etc

SYMPTOMATIC TREATMENT

They should be carried out on appropriate lines

PREVENTIVE MEASURES

The infestation by *T solium* may be prevented by (*a*) avoidance of eating uncooked or insufficiently cooked pork (*b*) rigid inspection of meat and supervision of the slaughter houses and (*c*) careful observation of personal hygiene Infected individuals should be promptly treated to guard against autoinfection otherwise they may suffer from cysticercosis In certain cases isolation of infected individual is justified

Tænia saginata

GEOGRAPHICAL DISTRIBUTION The infestation by this parasite occurs in countries where beef is eaten by the people Thus it is common in Eastern Europe Africa and in certain parts of India



FIG. 76 Ovum of *T saginata*

CAUSATIVE ORGANISM *Adult Stage* It is 4 to 15 metres in length thus much longer than the pork tapeworm The head has 4 suckers but is devoid of rostellum or hooklets The body has more than 1 000 segments which are more mobile and

muscular than those of *T solium* The uterus in the gravid segment has more than 13 lateral branches on each side of the central stem

Ova The eggs are round in shape about 30 to 40 *microns* in diameter and have a thin shell but a thick radially striated inner envelopes (Fig 26) enclosing the embryo with six hooklets and cannot be distinguished from those of *T solium*

Larval Stage (Cysticercus bovis) It occurs almost exclusively in the ox and extremely rare in man The cysticerci are found chiefly in the muscles of mastication of the ox

MODE OF INFECTION

Man becomes infected by ingestion of uncooked or insufficiently cooked beef containing the cysticerci The subsequent course is the same as described under *T solium*

CLINICAL MANIFESTATIONS

They are the same as those occurring in *T solium* It should be emphasized however that the stage of cysticercus bovis in man is very rarely seen

DIAGNOSIS

It is based on the detection of the characteristic segments and the ova in the stools

TREATMENT

Same as for *T solium*

PREVENTIVE MEASURES

Avoidance of eating uncooked or imperfectly cooked beef Other measures are the same as for *T solium*

Hymenolepis nana

GEOGRAPHICAL DISTRIBUTION This parasitic infection is common in India Japan America and Southern Europe



FIG 27 Ovum of *H nana*

AGE INCIDENCE Children are commonly affected

CAUSATIVE ORGANISM *Adult Stage* It is 10 40 mm long and has a head with four suckers and a rostellum with one row of hooklets The segments number 100 to 200

Ova The eggs are colourless oval 40 60 *microns* in diameter The inner membrane has mamillated projection with 2 4 filaments at

either end (Fig 27) It is usually found in larger numbers (100 1 000) in the small intestine of man mice and rats

MODE OF INFECTION

Man is infected by ingestion of food and drink contaminated with the egg which on reaching the mall intestine liberates the embryo It penetrates into the intestinal mucous membrane develops into a *cercocyst* which finds its way back to the intestine anchors itself to the villi and grows into the adult worm the segments of which liberate ova that are passed out in the fæces

CLINICAL MANIFESTATIONS

Vague intestinal troubles pain epigastrium acidity etc

DIAGNOSIS

It is made by detection of characteristic ova in the stools

TREATMENT

The treatment is very unsatisfactory Mepacrine hydrochloride ha been used but results are uncertain Bhaduri obtained encouraging results by using ca hew nut shell extract 6 g being used for adults

PREVENTIVE MEASURES

1 Healthy per ons should not share the same bed with the infected individual 2 Food and drinl should be protected against contamination with fæces of man rats and mice

Diphyllobothrium latum

GEOGRAPHICAL DISTRIBUTION It is found in man in northern Switzerland part of Germany in the Baltic countries and in Roumania

AGE AND SEX INCIDENCE No age is immune Both sexes are equally susceptible

CAUSATIVE ORGANISM *Adult Stage* It is white in colour 3 10 metres long with about 300 segments The scolex is small spatulate with a pair of sulci (*bothria*) dorsal and ventral The gravid segments are almost square In the chain of segments forming the body an opaque white spot is found in the middl of each segment due to the coiled uterus The eggs are light golden yellow in colour broadly oval operculated (Fig 28) and measure in average 66 by 44 *microns*

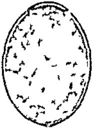


FIG 28 Ovum of *D latum*

Larval Stage The egg hatches in water in about 10 to 15 days and a hexacanth ciliated embryo comes out This embryo is swallowed by a copepod (*Cyclops Diaptomus*) in the hæmal cavity of which it develops into a pro cercoid larva The copepod is eaten up by a fresh water fish and the larva escapes and makes its way into the tissues and becomes a plerocercoid larva or *sparganum* On consuming this infected fish raw or underdone man acquires the infection

Mode of infection clinical manifestations diagnosis treatment and preventive measures are same as *H nana*

Echinococcus granulosus

[Tænia echinococcus]

GEOGRAPHICAL DISTRIBUTION It is prevalent in Iceland America Australia New Zealand Africa Arabia and is not uncommon in India

CAUSATIVE ORGANISM *Adult Stage* The adult is about 3 6 mm long It has a head with four suckers a rostellum with two rows of hooklets and four segments of which the last one is gravid and contain numerous eggs The uterus has short lateral branches The eggs are like those of tænia and the embryo has six hooklets The adult parasite inhabits the small intestine of dogs foxes and jackals

Larval Stage It occurs in sheep goat pigs cattle man horse and monkeys all of which may act as intermediate hosts Children under 10 years are especially susceptible

MODE OF INFECTION

Man and other intermediate hosts are infected by ingestion of food and drink contaminated with the eggs of echinococcus which are present in the fæces of infected dogs living in close contact with them Infection may also occur from the petting and kissing of dog The embryo (*onchosphere*) is liberated in the stomach and small intestine and penetrates through the mucous membrane It then passes into the portal bloodstream and after losing the hooklets settles down in the various organs such as liver (in 75 per cent of cases) lungs (in 15 per cent of cases) kidney peritoneum and brain forming hydatid cysts Such cysts may occasionally be found in the spleen heart spinal cord eye bones muscles and subcutaneous tissues The mature cyst has two layers *i.e.* (*a*) an outer laminated layer (*ectocyst*) secreted by the cyst and (*b*) an inner germinal layer (*endocyst*) from which brood capsules daughter cysts and grand daughter cysts are formed by endogenous budding Surrounding the hydatid cyst there

is a layer of fibrous tissue (*pericyst*) derived from the tissues of the host. Each brood capsule about the size of a pin's head gives rise to a number of *scolices*. Brood capsules may be formed also by a process of exogenous budding as in the bones. The multilocular cysts are due to atypical development and may be due to a second parasite *E. multilocularis*. The cyst grows in size and may become as big as a child's head. The hydatid fluid is a clear watery liquid of a specific gravity of 1004-1010 containing sodium chloride, dextrose, cholesterol and a little protein. Scolices and hooklets may be present in the fluid.

CLINICAL MANIFESTATIONS

In the early stages there may not be any symptoms for years. The symptoms usually vary according to the site of the hydatid cyst and its size. They are as a rule produced by (*a*) pressure of the growing cyst on important structures, (*b*) atrophy and necrosis of the tissues surrounding the cyst, (*c*) infection and suppuration of the content of the cyst, (*d*) accidental rupture of the cyst giving rise to anaphylactic symptoms and later on to formation of secondary hydatid cysts at the sites of implantation of the liberated scolices.

Retrogression of symptoms with spontaneous cure may result in 30 per cent. of hydatid cysts of the liver due to the death of the parasites and subsequent calcification.

DIAGNOSIS

CLINICAL DATA. 1. History of close contact with dogs. 2. Occurrence of frequent urticarial eruptions with fever. 3. Presence of a *hydatid thrill* over the cysts in liver and peritoneum. 4. Presence of eosinophilia. 5. Occasional presence of cysts, membranes and scolices in the sputum, stools and urine.

LABORATORY DATA. 1. The intradermal test (*Casoni's test*). It is extremely valuable because it has been found to be positive in 90 per cent. of hydatid cases. The occurrence of a large wheal surrounded by a zone of erythema and œdema in the skin in half an hour (*immediate reaction*) or in 6 to 8 hours (*delayed reaction*) after intradermal injection of 0.2 c.cm. of filtered sterile hydatid fluid obtained from sheep indicates a positive reaction. 2. Microscopical examination. Detection of scolices, membranes and hooklets in the fluid obtained on exploratory puncture. 3. Complement fixation test. 4. Precipitin reaction.

Radiological examination of the suspected organ shows the characteristic cricketball like shadow in large unruptured cysts.

TREATMENT

No specific drug is available for eradicating the parasite

Treatment is essentially surgical No attempt to drain the contents of the cysts should be made unless scolices have been killed by a preliminary injection of formalin into the cyst Symptoms are treated as they arise

PREVENTIVE MEASURES

The following are the chief preventive measures

1 Strict observance of the hygienic rules 2 Avoidance of too much petting of dogs 3 Careful washing of hands after touching dogs 4 Quarantine of all dogs for 1 2 days once or twice a year during which they are properly bathed and treated with drugs 5 Rigid supervision of slaughter houses 6 Regular inspection of all meat 7 Proper disposal of all infected organs of sheep and goat by burning

N V B

CHAPTER XI

FILARIASIS

DEFINITION

Filariasis is a disease caused by certain nematode worms of which *Wuchereria bancrofti* is the most important and clinically characterised by attacks of periodic fever lymphangitis chyluria various forms of lymphatic varix and elephantiasis In India *W bancrofti* and *W malayi* are responsible for filariasis Both varieties of parasites can occur in the same person

HISTORY

In 1863 the larval form of the parasite was found by Demarquay in milky hydrocele fluid In 1866 Wucherer found it in chylous urine In 1872 Lewis in India discovered that human blood stream is the normal habitat of the microfilaria and he named it *Filaria sanguinis hominis* In 1876 Bancroft discovered the adult form and named it *Filaria bancrofti* In 1878 Manson discovered that the mosquito played the role of intermediary host and two years later he pointed out the nocturnal periodicity of the microfilaria in the peripheral circulation and called these embryonic forms *Filaria nocturna* which name was subsequently changed to *Microfilaria bancrofti* Manson Bahr showed that five or six different species of microfilaria may inhabit human blood Brug described the *Mf malayi* in 1927 and Rao & Maplestone discovered and described the adult *W malayi* in 1940

In some of the Pacific islands microfilariæ found in man do not exhibit nocturnal periodicity and tranmission occurs through a different mosquito For these reasons Manson Bahr has proposed to name the adults *W pacifica* though these are morphologically similar to *W bancrofti*

Filariasis due to W bancrofti

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is found throughout the tropical and sub tropical countries It is common in North Africa Southern Spain South America the West Indies Southern China North Australia and the Pacific Islands It is very prevalent in certain coastal and riverine areas of India These areas

may be hyperendemic moderately endemic or slightly endemic according as the microfilaria rate is 20 per cent or over between 10 and 19 per cent and under 10 per cent respectively in the population (*Acton* and *Rao*) Thus Cochin and parts of Puri and Cuttack constitute the hyperendemic areas Calcutta and Purulia are the endemic areas and Allahabad is an area of low endemicity

AGE SEX AND RACE INCIDENCE It is rarely seen in children under 12 to 15 years of age except in the hyperendemic areas The incidence increases after the 20th year It occurs more commonly in males than in females All races seem to be equally susceptible

CAUSATIVE ORGANISM The adult *W bancrofti* worms are responsible for the pathological conditions in filariasis and no sign or symptom is due to microfilariae whose presence in the peripheral blood is certainly a source of great danger to others

Adult Stage The adults are long thread like *W bancrofti* male about 40 mm in length and 0 1 mm in breadth is much smaller and thinner than the female which measures about 100 mm in length and about 0 25 mm in breadth The two uterine tubes of the female worm contain numerous ova in all stages of development and open at the anterior end Both male and female live coiled together either in the cyst like dilatations of the distal lymphatics of the limbs or the large retroperitoneal lymphatic trunks in the thoracic duct or in lymphatic glands themselves behind the peritoneum or in the groins As a matter of fact they may be found in the dilated lymphatics in any part of the body *e g* extremities external genitals mammary glands etc While inside the glands or lymphatics they are actively motile they die within a few hours if removed from the body A large number of worms may live in a bunch in one place The duration of life of the adult worm may be several years It is calcified after its death and remains within the body in this condition in the lymphatics or in the glands

Larval Stage The microfilaria which is a thin cylindrical snake like organism measures about 0 25 mm in length and 7 5 to 9 *microns* in breadth and so it can pass through the capillaries It is enclosed in a sheath (Fig 29) within which it constantly moves forwards and backwards

As long as the adult worm in the lymphatics communicates directly with the blood stream the microfilariae will be seen in the peripheral blood and may be present in such a large number that one drop of blood on the slide may sometimes show about 100 parasites if taken at the

proper time It was first pointed out by Manson that the microfilariæ disappear from the peripheral blood stream during daytime and reappear at night (*nocturnal periodicity*) They begin to appear in the peripheral blood toward the evening after which they steadily increase in number reaching the maximum at about midnight to 2 a m Then gradually they begin to fall in number reaching the minimum about early morning and completely disappear with sunrise or immediately after The cause of this nocturnal periodicity is not clearly understood The following are some of the theories which have been put forward to explain this periodicity

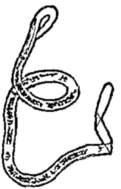


FIG. 29 Microfilaria of *W bancrofti*

1 The microfilariæ appear in the blood at night to adapt themselves to the nocturnal habits of their intermediate host *Culex fatigans* which is responsible for their propagation The Pacific microfilariæ appear in the peripheral blood in the daytime corresponding to the day habits of their intermediate host *Aedes pseudoscutellaris*

2 The microfilariæ may find some difficulty in passing through the capillaries of skin and lungs due to their contracted condition during the day's activity but during sleep at night the capillaries regain their normal condition and allow the microfilariæ to circulate in the blood stream without any difficulty or obstruction The fact that the microfilariæ appear during daytime in the blood of persons sleeping in the day and disappear at night if they keep awake at night is in favour of this explanation

3 Some workers (*Law* and *O Connor*) hold that all the microfilariæ present in the blood perish in 24 hours and their periodical appearance is the result of simultaneous periodical parturition of the adult female worms But the life of the microfilaria is longer than 24 hours and may be as long as ten weeks (*Rao*)

MODE OF INFECTION

There are several species of mosquitoes which serve as intermediate hosts and the female of *Culex fatigans* is responsible for the transmission of the disease in India

The mosquito biting an infected person sucks blood containing a large number of microfilariæ which escape from their sheaths in the stomach aided by the viscidity of the ingested blood and by their own active movements Then they penetrate through the stomach

wall into the thoracic muscles where they undergo further development and acquire the internal structures of the infective stage the whole process taking about 10 to 40 days to complete according to the atmospheric condition temperature and humidity A relative humidity of over 60 per cent and a temperature of 80° 90°F are most favourable for the development of the filarial embryos in the mosquito (*Rao* and *Iyengar*) The filariform larvæ find their way into the proboscis and usually remain in pairs When the infected mosquito bites a man these microfilariæ escape on to the skin of the man through the thin membrane of the labium It is not definitely known whether they penetrate the skin near about the point of bite to enter the body of the definitive host or they enter through the mosquito made puncture On gaining access to the body they reach the lymph stream where they settle down at some spot grow and attain sexual maturity before entering the nearest lymph node when they begin in due course to produce new generations of embryos

A mosquito biting a man who carries numerous microfilariæ in the peripheral blood is likely to develop a heavy infection and die So a heavily infected person is less dangerous to the society than the lightly infected one

PATHOLOGY

The pathological lesions in filariasis are produced by the adult filariæ Microfilariæ as a rule are non pathogenic The production of the lesions is primarily dependent on an obstruction to the lymph flow This lymphatic obstruction is the result of cellular reactions such as giant cell formation eosinophilic infiltration fibroblastic proliferation and fibrotic changes set up in the lymph nodes by the irritant action of adult worms which may be alive or dying and by the persistent disintegration of microfilariæ through the activity of the reticulo endothelial cells during their passage through the afferent lymph stream of the proximal lymph nodes Occlusion of the lymphatic vessels due to the endothelial proliferation may also lead to lymph stasis The progressive lymphatic obstruction causes

(*a*) Dilatation of the lymphatics leading to varicose lymphangiomatous swelling in the groin or axilla (varicose groin or axillary glands) or in the spermatic cord (lymphatic varicocele)

(*b*) Chylous exudation into the various serous sacs *e g* pleura peritoneum pericardium and the tunica vaginalis giving rise to chylothorax chylous ascites chylopericardium and chylocele or hydrocele respectively

(*c*) Rupture of the lymphatic varices into the walls of the urinary tract (*chyluria lymphuria*) the walls of intestine (*chylous diarrhœa*) into the peritoneal cavity (*chylous ascites*) into scrotal skin (*lymph scrotum*)

Secondary bacterial infection from septic foci is believed to be superimposed on lymph stasis causing inflammatory reactions in various tissues *e g*

1 Lymphangitis
2 Lymphadenitis
3 Epididymo orchitis and funiculitis
4 Filarial abscesses which may occur in the skin and subcutaneous tissues of the limbs the pelvis of the kidney the inguinal glands epididymis the retroperitoneal tissues and the tissue around the spermatic cord

Allergic reactions in response to the liberation of the metabolite of the living worms and disintegrating products of the dead worms have recently been suggested to cause inflammatory changes in the obstructed lymphatics and lymph glands (*O Connor*)

Microfilarial granulomata have recently been described in the spleen by Dhayagude and Amin They appear on the cut surface of the spleen as multiple circumscribed reddish brown nodules caused by the presence of microfilariæ with marked engorgement of the splenic sinuses reticulo endothelial hyperplasia giant cell formation and eosinophilic infiltration

CLINICAL MANIFESTATIONS

In cases without any lymphatic obstruction the adult filariæ may live as long as ten years or more in the glands or lymphatics and produce no clinical manifestations The only evidence of the toxic effect of the infection in such cases is a moderate degree of eosinophilia

In others associated with lymphatic obstruction and lymph stasis the symptoms are variable depending on the intensity of infection and the site of lymphatic blockage They may conveniently be described as below

FILARIAL LYMPHANGITIS AND FILARIAL FEVER Lymphangitis is very frequently seen in filarial subjects as a result of a secondary infection by *Streptococcus hæmolyticus* and when it affects the superficial lymphatics of any part of the body especially limbs painful swelling of the lymph vessels which are cord like in feel erysipeloid inflammation of the *superjacent* skin and swelling of the associated glands are noticed There is a sudden onset of high fever with rigor

and sometimes vomiting along with these inflammatory conditions in the affected area There may be filarial fever without any obvious lymphangitis due to involvement of the deep seated abdominal lymphatics or glands The fever with the accompanying local conditions may continue for several (3 to 5) days severe headache vomiting loss of appetite quick pulse delirium and other marked constitutional symptoms may be present The blood examination shows marked leucocytosis 20 000 40 000 per c mm with an increase of polymorphonuclear cells Then the temperature comes down to normal by crisis with profuse sweating the swelling gradually subsides and the attack comes to an end Repeated attacks of this kind are liable to occur at varying intervals When such acute lymphangitis occurs in an extensive abdominal varix the symptoms may simulate those of peritonitis and it may prove fatal In some cases inflammation occurring in the deeper lymphatics may occasionally result in the formation of an absce

LYMPH SCROTUM The scrotal skin which is thick reddish brown and velvety shows a large number of pea sized vesicles which discharge a clear or chylous fluid amounting to several ounces in the whole day and often containing microfilariæ and yielding *streptococci* and *staphylococci* on culture This discharge may persist for days and give rise to an eczematous condition of the scrotum Lymph scrotum may be associated with lymphangitis and periodic febrile attacks In most cases of lymph scrotum there is a history of previous operation for the radical cure of hydrocele Moreover lymph scrotum is often followed by scrotal elephantiasis

FILARIAL ELEPHANTIASIS (*Elephantiasis arabum*) It is a condition of hyperplasia and hypertrophy of the skin and subcutaneous tissues associated with a *solid or non pitting œdema* caused by repeated attacks of superficial or deep seated lymphangitis due to a secondary bacterial infection superimposed on an almost complete occlusion of the lymph channels by the dead adult filariæ and the process of calcification and fibrosis around them

Elephantiasis is often seen in the legs (in 95 per cent of cases) and the scrotum The thighs arms penis vulva and rarely the breasts may be affected In the early stage the disease is characterised by attacks of fever (*elephantoid fever*) associated with lymphangitis and regional lymphadenitis The affected parts are gradually swollen the skin becomes thickened and the hairs get scanty In elephantiasis of the leg the swelling may be enormous but does not usually extend upwards beyond the knee The elephantoid tumours

of the scrotum vulva and the breasts may be very large and thus cause mechanical difficulties and much mental depression

Because of the lymphatic blockage and perhaps the death of the adult parasites in some instance though the microfilariae are often absent in the peripheral blood stream the eosinophil count is usually normal or only slightly raised In the Fijian cases of elephantiasis Man on Bahr has reported the presence of microfilariæ in the peripheral blood in 38 2 per cent Histological examination of the elephantoid tissues will often show the remnants of the adult filariæ X ray examination of the elephantoid parts may show the presence of calcified worms (O Connor)

VARICOSE GROIN GLANDS The inguinal or femoral glands on one or both sides are enlarged and have a soft doughy feel The skin over the affected glands is freely movable The glands do not rapidly diminish in size on lying down Periodic febrile attacks with pain and lymphangitis are not uncommon The condition may be associated with lymph scrotum hydrocele or chyluria

CHYLURIA It is characterised by the passage of white milky urine due to rupture of the distended lymphatics in the walls of the pelvis of the kidneys ureters or urinary bladder as a result of lymphatic obstruction at the level of the juxta aortic group of lymph nodes or the cisterna chyli which is usually seen amongst persons residing in areas of low endemicity for over 20 years

Exciting Factors In females the disturbance of the pelvic lymphatics in pregnancy and the strain and muscular efforts during child birth help in the causation of the rupture of the distended lymph vessel In infected males violent exercises *g* running riding jumping etc or any accidental injury on the loins or pelvis may be responsible for the occurrence of the condition

Clinical Features Chyluria has often a sudden onset and may have an equally sudden termination An attack may continue for days weeks or month and one day all on a sudden the urine may be perfectly clear without any apparent cause Pain in the back and kidney regions and a dull aching sensation in the pelvis and groin may be felt due to distension of the lymphatics Dysuria or a complete retention of urine may occur due to coagulation of the chyle in the bladder and blocking of the urinary passage

The urine may be white like milk pinkish or even red or at times especially in the morning absolutely clear like normal urine The colour of the urine varies from day to day and even in 24 hours depend

ing on the nature of food and temporary closure of the rupture in the lymphatics Pinkish or red colour indicates presence of blood, which may come from rupture of small blood vessels into the distended and leaking lymphatics or from the diapedesis of blood corpuscles into the lymph retained long in the varicose lymph vessels

A sample of freshly passed chylous urine kept in a conical urine glass for some time coagulates and within one or two hours separates into three layers having a cream like pellicle at the top small granular reddish sediment at the bottom and a coagulum floating in the middle of the milky fluid

The sediment shows on microscopical examination red blood corpuscles lymphocytes epithelial cells granular fatty matter and in many cases a number of microfilariæ The upper and the middle layers *contain granular fatty material The coagulum also shows microfilariæ*

On chemical examination the urine is found to contain a large amount of fat and albumin If the milky urine is shaken well with ether the fat particles get dissolved and the urine turns clear

Chylous urine should be differentiated from chyliform urine and pseudochylous urine *Chyliform urine* is not due to obstruction in the lymphatics It contains fat which is shown by the urine clearing up when shaken with a few drops of ether Chyliform urine is due to diabetic lipæmia or fatty degeneration of any growth in the kidney bladder or elsewhere in the urinary tract No microfilariæ are found in the urine or blood *Pseudochylous urine* looks milky not due to fat but due to the presence of a lecithin compound of globulin or an excess of globulin and so it does not clear up with ether It is also due to *degenerative changes and not due to blockage in the lymphatics* No microfilariæ are seen in the urine or blood

Though chyluria is not dangerous to life yet in longstanding cases it may produce anæmia debility and mental depression The condition is generally afebrile

COMPLICATIONS

A patient may show one group of clinical manifestations to begin with and he may develop any time in course of the disease other groups of symptoms

There is one particularly serious complication which is liable to occur in filarial subjects and that is *acute funiculitis* with *secondary invasion of the blood stream* by *Streptococcus hæmolyticus suppurative peritonitis* and formation of minute *abscesses in the lungs* Banerjea has noted one case of this nature verified at autopsy

Besides those already mentioned there may be other complications such as

1 Suppurative orchitis

2 Acute bacterial endocarditis Such a lesion of the pulmonary valves in course of a septicæmia due to *Streptococcus hæmolyticus* superimposed on acute filarial orchitis and funiculitis has been described by De and Chatterjee

3 Synovitis and fibrous ankylosis of the joints

4 Iridocyclitis rarely An adult *W bancrofti* has been reported to be removed from the anterior chamber of the eye (*Chatterjee*)

PROGNOSIS

The expectation of life is not reduced and septic complications are more easily controlled with modern treatment Serious deformities may arise in persons exposed to repeated infections for many years

DIAGNOSIS

CLINICAL DATA 1 Residence in an endemic area in the tropics 2 Presence of one or more of the following filarial manifestations (*a*) Lymphangitis associated with fever (*b*) Elephantiasis (*c*) Enlarged and tender epitrochlear and superficial inguinal lymph node (*d*) Lymph scrotum (*e*) Varicose groin or axillary glands (*f*) Chyluria 3 Periodic febrile attacks at intervals of weeks or months

LABORATORY DATA 1 Blood examination showing (*a*) presence of a moderate or high eosinophilia (*b*) presence of microfilariæ

2 Examination of urinary sediment in a case of chyluria may show the microfilariæ

3 Examination of the fluid aspirated from the hydrocele sac enlarged lymph nodes dilated lymphatics and filarial abscesses for microfilariæ About 10 per cent of cases of primary hydrocele show microfilariæ in the hydrocele fluid (*Rao*) Adult filariæ usually dead but sometimes alive may be detected on a careful examination of the pus from filarial abscesses excised lymph glands and the serous fluid from the lymphatic cysts

4 Intradermal test (*Fairley*) It is helpful in distinguishing the non filarial type of elephantiasis from the filarial type It is done in the same way as in hydatid disease The antigen consists of an extract of *Dirofilaria immitis* of the dog

5 Complement fixation test with the antigen of *Dirofilaria immitis* The test is however negative in cases of chronic elephan

tiasis with lymphatic obstruction and lymphangitis due to a secondary bacterial infection

6 Occasional demonstration of calcified filariæ in the tissues of the limbs on a radiological examination

Methods of Detection of Microfilariæ in Blood

(*a*) *Wet method* (i) A drop of blood is taken on a slide by pricking the finger tip of the patient between 10 p m and 2 a m while the patient is asleep in a dark room The drop of blood is covered with a coverslip the margins of which are smeared with vaseline to prevent drying of the blood film The wet film is examined under the low power of the microscope immediately or next morning (ii) While the patient is sleeping in a dark room one to two c cm of blood is taken from a vein into a test tube containing about 5 c cm of a 2 per cent solution of sodium citrate or acetic acid The blood is centrifuged next morning and the deposit is examined on a slide under the microscope The writer is of opinion that it is better to take the blood by saponin solution and centrifuge it for detection of microfilaræ in the deposit This method gives better result

(*b*) *Staining method* One or two large drops of blood are taken from the tip of a finger in the usual hour and spread over an area of half a square inch on a slide and kept covered Next morning when the film is dry it is dehæmoglobinised and stained with Leishman stain or Giemsa or a dilute watery solution of fuchsin or methylene blue and examined under the microscope

DIFFERENTIAL DIAGNOSIS

Filarial Fever is to be distinguished from

MALARIA (See under Malaria)

Filarial Lymphangitis should be differentiated from

SEPTIC LYMPHANGITIS 1 Ascending lymphangitis 2 Septic source

THROMBO PHLEBITIS MIGRANS 1 Presence of the migratory character 2 Absence of eosinophilia

Varicose Groin Glands may have to be differentiated from

BUBONOCELE 1 Slow disappearance of the swelling on lying down and its slow appearance on standing up 2 Presence of an impulse on coughing 3 Presence of a tympanitic note on percussion a feature which is also present in an omentocele

Filarial Elephantiasis has to be differentiated from

DIFFUSE FIBROMATOSIS (*Von Recklinghausen's syndrom*)

1 Neurofibromata can be felt along the course of the cutaneous nerves 2 Scalp face and buttocks are affected 3 Presence of pigmented patches

ANGIONEUROTIC ŒDEMA (*Quincke's disease*) 1 Presence of hereditary history 2 Face is commonly affected 3 Occurrence sudden and painless 4 Presence of sensitiveness to articles of diet or drugs

HEREDITARY ŒDEMA (*Milroy's disease*) 1 Presence of hereditary or familial incidence

HYPOPITUITARISM (*Dercum's disease*) 1 Stunted growth and emotional instability 2 The affection is limited to the proximal parts of the arms buttocks and flexor surfaces of the thighs 3 Presence of painful fatty lumps

ELEPHANTIASIS NOSTRAS 1 Presence of septic conditions in the feet or puerperal sepsis 2 Involvement of face and lips

EPIDEMIC DROPSY 1 Epidemic outbreak 2 Affection in other members of the family 3 Presence of cardiovascular symptom glaucoma blotchy cutaneous erythema and epidemic dropsy nodules

GENERAL MANAGEMENT

Rest in bed is indicated in cases with lymphangitis elephantoid fever lymph scrotum and chyluria The bowels should be attended to An adequate nourishment should be maintained by appropriate diet Limitation of fats and fluid intake is essential in chyluria

EXERCISE Patients with chyluria should avoid undue exertion

ELIMINATION OF SEPTIC FOCI All septic foci in gums teeth tonsils sinuses skin and bowels should be eradicated as far as practicable Immunisation by autovaccines made from the predominating organisms of such foci is helpful

SPECIFIC TREATMENT

Few drugs have been found that may have a specific action on the adult worms Antimony preparations given in intensive doses are believed either to kill the parent worm or to render them sterile These preparations when used for the treatment of canine filariasis have been found to affect the adult worms Clinically in human beings the effect is seen by gradual disappearance of the filarial embryos from

the peripheral blood Very recently piperazine derivatives (1 diethyl carbamyl-4 methyl piperazine hydrochloride or citrate) have been found to be very effective in removing microfilariæ from the peripheral blood

1 ANTIMONY PREPARATIONS (*a*) *Sodium Antimony Tartrate* A 2 per cent solution of sodium antimony tartrate in 2 to 5 c cm doses intravenously has been reported to reduce the number of microfilariæ in the blood and improve the clinical condition but the same drug has been tried by other workers with negative results

(*b*) *Lithium Antimony Thiomalate* This is a trivalent antimony preparation (*anthiomaline*) It is used intramuscularly every day The initial dose is 1 c cm and the maximum daily dose is 3 c cm and usually a total dose of 60 c cm is used The injections are rather painful and accompanied with moderate toxic symptoms like urticaria epigastric pain nausea vomiting skin eruptions joint pains etc Nevertheless the results are reported to be very encouraging

(*c*) *Fouadin* a trivalent antimony preparation has been used in 1½ to 5 c cm doses intramuscularly biweekly till a total dose of 40 c cm is reached The drug is rather toxic The results are reported to be encouraging

(*d*) *Neostibosan* 0 3 g on alternate days for 5 7 weeks has also been used with some success

(*e*) *Stibatin Concentrated* containing 100 mg of antimony gluconate per c cm may be used starting with an initial dose of 1 c cm and increasing to 4 c cm daily by the intramuscular route An average of 15 to 20 injections is used

2 ARSENICAL PREPARATIONS (*a*) *Novars nobillon sulpharsenol sodium cacodylat soamin* etc have been tried with occasional good results Soamin is given in 1 grain dose intramuscularly every second or third day a total of gr 15 to 20 being injected

(*b*) *Tryparsamide* (a pentavalent arsenical) is according to some authorities a valuable drug in the treatment of chyluria It is given intravenously once a week in 2 g doses dissolved in about 10 c cm of sterile water In some cases one or two injections of the drug clear up the urine but the writers have experienced failure of the drug to control the condition in many cases

Arsenicals should never be used indiscriminately as it may cause optic atrophy

3 IODINE PREPARATIONS (*a*) *Potassium Iodide* has been suggested to help the absorption of the inflammatory thickening which

causes the obstruction in the lymphatics (*b*) *Iodine* given intravenously is said to be beneficial in some cases

4 PROTEIN SHOCK THERAPY (*a*) *Vaccine* made from *strepto cocci* and *staphylococci* isolated from the septic teeth gums tonsils skin and bowels has been extensively used and well reported for the suppression of filarial attacks in non allergic patients

Dose 1 c cm contains *streptococci*—50 millions and *staphy lococci*—250 millions

The initial dose is 0 1 c cm and it is increased by 0 1 c cm till a dose of 1 c cm is reached depending upon the focal and local reactions Injection should be given every third or fourth day intra d rmally upto 0 3 c cm and then subcutaneously When the dose of 1 c cm is reached it can be given at longer intervals *e g* once a week The vaccine treatment in most of the case has been found to be of value in preventing the recurrent attacks of lymphangitis and filarial fever

(*b*) *T A B Vaccines* have also been suggested by some workers as a non specific protein therapy in filariasis but the result is not uniformly promising

(*c*) *Special Antifilarial Vaccin* containing streptococci staphy lococci and *Esch coli* in solution of a stable organic arsenical com pound (soamin) given intramuscularly or intravenously in graduated doses has also been used with variable results

5 HETRAZAN It is a new synthetic organic compound *Banocide* is a similar preparation This drug removes microfilariæ from peripheral blood very rapidly but it is doubtful whether it has got any significant action against the adult forms of *Wuchereria bancrofti* or *W malayi*

Dose It is available as 50 mg tablets and is administered by the oral route The optimum dose is 2 mg per kilogram of body weight three times daily after meals and continued for 3 weeks

Though the drug causes disappearance of microfilariæ from peripheral blood the clinical signs and symptoms of filariasis which are usually produced by adult worms seldom show amelioration The drug however has a very promising future for reducing the number of carriers in mass prophylaxis The drug is fairly nontoxic Systemic allergic reactions which may occur during treatment are probably caused by the liberation of filarial protein when the microfilariæ are

killed Cases with *Mf malayi* in blood showed a good degree of reaction (Wilson) Symptoms like slight nausea anorexia fever lassitude malaise and headache are caused by the drug itself but all these symptoms are transient

SYMPTOMATIC TREATMENT

LYMPHANGITIS 1 Elevation of the affected part

2 Application of cooling lotions such as Coulard's lotion or hot fomentation

3 Application of ethyl chloride spray over the palpable nodules in course of the inflamed lymphatics may check the progress of the disease

4 Relief of pain by aspirin Dover's powder or morphine and its derivatives

5 Treatment of the associated fever by adequate doses of alkali mixtures and sulpha or penicillin are often successful because the secondary infection is usually of streptococcal origin

6 Use of autogenous vaccines

7 X ray treatment may be tried

8 Use of diamino-diphenyl sulphone in 50 mg dose daily for 3 to 6 months is helpful in suppressing attacks of filarial lymphangitis (*Bhaduri*)

CHYLURIA 1 Elevation of the pelvis to relieve the distended lymphatics

2 Restriction of fats and also of fluids unless there is dysuria with retention of urine

3 Relief of retention of urine if there be any by catheterisation under aseptic precautions and washing out of the bladder with mild antiseptic lotion

4 X ray irradiation of the kidneys—reported to be beneficial by Golden and O Connor and by Bhaduri

5 Use of arsenic and antimony preparations—beneficial

6 Use of prednisolone is sometimes helpful

VARICOSE GROIN GLANDS Avoidance of surgical interference as far as practicable

LYMPH SCROTUM 1 Local medication with rest in bed

2 Local x ray therapy may be helpful

ELEPHANTIASIS 1 Elevation of the affected part and its support by elastic bandages

2 Avoidance of injury and secondary infections

3 Periodic administration of autogenous mixed streptococcal and staphylococcal vaccines

4 Adoption of operative procedure to promote lymphatic drainage

ELEPHANTOID TUMOURS Appropriate surgical treatment

ACUTE FUNICULITIS 1 Early administration of antibiotics followed by sulpha drugs in optimum dosage in hyperacute cases

2 Hot fomentations

3 Incision and drainage in case of suppuration

ANAEMIA AND DEBILITY Administration of large doses of suitable iron salts and general tonics

PREVENTIVE MEASURES

Protection against infection is ensured by

1 The routine use of mosquito net at night throughout the period of residence in an endemic area

2 Adoption of anti mosquito measures

3 Mass treatment with hetrazan appear to have a promising future in eradicating human carriers

Filariasis due to W malayi

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION Filarial infection due to *Wuchereria malayi* is prevalent in Malaya Dutch East Indie South China Indo-China Ceylon and India (North Travancore Assam Orissa Madras and Bengal)

AGE INCIDENCE The incidence increases with age

CAUSATIVE ORGANISM The adult *W malayi* and not the *Microfilaria malayi* is responsible for the pathological lesions

Adult Stage The general appearances are similar to those of *W bancrofti* The male is 22 23 mm long and 0 08 mm broad The female is 55 mm long and 0 16 mm broad The course of the uterus and its branches is the same as in *W bancrofti* The female of *W malayi* is practically identical with that of *W bancrofti* but the male of this species differs from that of *W bancrofti* in the tail papillæ and in the spicules which are much more delicate than those of the latter and the transverse corrugations on the stout portion of the spicules are not so prominent as in *W bancrofti* (*Rao* and *Maplestone*)

The adults both male and female live coiled together in the dilated lymphatics

Larval Stage The *Microfilaria malayi* was first described by Brug in 1927 It is distinguished from *Microfilaria bancrofti* by its more clumsily aggregated nuclei deeper cephalic space easily visible anal pore and the tail with 1 2 nuclei

MODE OF INFECTION

The infection is conveyed to man by the bite of *Mansonioides annulifera* in which the development of *Microfilaria malayi* takes place

PATHOLOGY

Same as in filariasis due to *W bancrofti*

CLINICAL MANIFESTATIONS

The earliest clinical manifestation is lymphadenitis especially of elbows and the groins Lymphangitis with a definite periodicity is often seen Elephantoid lesions invariably affect the superior and inferior extremities The elephantiasis which occurs in comparatively young persons especially males in the hyperendemic areas is not so huge as in *W bancrofti* infection Affection of genital organs and chyluria are not found in areas where only *W malayi* infection occurs

TREATMENT

Same as in filariasis due to *W bancrofti*

PREVENTIVE MEASURES

It may be successfully carried out by (1) adoption of anti mosquito measures against *Mansonioides annulifera* and (2) eradication of the plant *Pistia stratiotes* from the endemic area (*Sweet* and *Pillai*) and (3) use of appropriate dose of piperazine compounds at intervals of six months or so

N V B

CHAPTER XII

DRACONTIASIS

[Guinea worm disease]

DEFINITION

It is a disease caused by a nematode *Dracunculus medinensis* (*Filaria medinensis*) characterised by the development of subcutaneous swelling blister or ulcer especially in the lower limbs

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It occurs frequently in tropical Africa Arabia Turkestan Iran and the eastern and western coasts of India where there is scanty rainfall and scarcity of drinking water

CAUSATIVE ORGANISM *Adult Stage* The female is 40 120 cm long and 0 5 1 5 mm broad It is whitish in colour cylindrical with a slightly tapering anterior end and faint transverse striations The large uterus occupies almost the whole body and is filled up with numerous embryos The male which is rarely found is very small 20 30 mm long It dies soon after copulation which probably takes place in the retroperitoneal connective tissues

Larval Stage Each of the larvæ about 0 6 mm long and 0 02 mm broad has a flattened finely striated coiled up body with long tapering tail On being discharged into water they swim about actively until they enter into the body of a fresh water crustacean (*cyclops*) the intermediary host in which after moulting 2 3 times and shedding their tails they develop each into a larva 1 mm long in 4 6 weeks

MODE OF INFECTION

The infection is conveyed to man through drinking water containing the infected cyclops which liberate the larvæ as a result of the digestive action of the gastric juice Then the actively motile embryos penetrate through the intestinal walls and reach the retroperitoneal tissues of the definitive host where they attain maturity in about one year

PATHOLOGY

When the embryos inside the female worm attain maturity it begins to migrate downwards to the subcutaneous tissues of the lower

limbs Here it may come near the surface around the ankle and form by the irritant action of its toxic secretion a small blister which may ultimately rupture giving rise to an ulcer At the base of this ulcer there is a minute pore through which an exudation of fluid at first clear and later milky occurs in response to the stimulus of cold water Sometimes the head of the worm or the uterus may protrude out of this pore The milky fluid which exudes out of the pore or from the ruptured prolapsed uterus contains numerous larvæ of *D medinensis* *In course of ten to fifteen days the worm empties its uterus completely* of all the embryos and escapes through the ulcer spontaneously or aided by gentle traction If traction is however, applied prematurely before the complete expulsion of the embryos and the body of the worm is injured the liberation of the embryos and the body fluid occurs in the subcutaneous tissues causing serious inflammatory changes leading to acute cellulitis and abscess formation due to allergic reaction and secondary pyogenic infection Synovitis arthritis buboes and epididymitis may also occur The invasion of the blood stream by hæmolytic streptococci and staphylococci is not uncommon

If during migration the worm fails to reach the surface of the body it dies in the tissues and undergoes calcification

CLINICAL MANIFESTATIONS

During the stage of growth or of migration there may not be any symptoms except occasional attacks of localised or generalised urticaria The formation of the blister or the ulcer is preceded by certain prodromata such as vomiting diarrhœa urticarial eruptions dyspnœa and collapse Blood examination may reveal eosinophilia The ulcer is situated at the lower extremities in 86 5 per cent of cases (*Fairley*) Less frequently it may be found in the scrotum occasionally in the arms and very rarely in the head

In case of secondary infection by streptococci staphylococci or *Esch coli complications such as cellulitis and abscesses may* occur Calcification of the dead worms may give rise to symptoms of muscular rheumatism or sciatica The calcified worms may be seen by the x rays as convoluted moniliform shadows or linear opacities

COMPLICATIONS

1 Septic complications such as cellulitis abscess buboes epididymitis purulent arthritis (especially of the knee joints) and sometimes *septicæmia* 2 Allergic complications such as synovitis and arthritis especially of the knee joints

SEQUELAE

1 Subacute sterile abscesses—due to premature death of the worm with liberation of the larvae in the subcutaneous tissues 2 Contractures of tendons 3 Ankylosis of joints

PROGNOSIS

In absence of secondary bacterial infection the course of the disease is mild and mortality is almost nil

DIAGNOSIS

In most cases the diagnosis is obvious from the following data and history of residence in an endemic area

CLINICAL DATA 1 Presence of an ulcer in the lower limbs discharging milky fluid or showing the prolapsed uterus of the worm in response to the stimulus of cold water

2 Presence of a beaded cord like feeling in the skin due to the worm underneath

LABORATORY DATA 1 Eosinophilia 2 Positive intradermal test (*Ramsay*) showing in 85 per cent cases a wheal 2 3 cm in diameter at the site of intradermal injection of a suitable antigen made from the dried powdered *D medinensis* in dose of 0 25 c cm

RADIOLOGICAL EXAMINATION 1 Screening after injection of 2 c cm of 10 per cent collargol or lipiodol into the worm to render it opaque is helpful in visualizing the course of the worm

2 Skiagram may show the calcified worms

SPECIFIC TREATMENT

There is no specific remedy against the guinea worm Intravenous injections of tartar emetic have not proved to be of much valu

SYMPTOMATIC TREATMENT

BLISTER AND ULCER A blister if any requires aspiration An ulcer should be treated with antiseptic dressings to prevent secondary infection

ALLERGIC SYMPTOMS Hypodermic injection of $\frac{1}{4}$ to $\frac{1}{2}$ c cm adrenaline chloride solution 1 in 1000 The antihistaminic drugs (as *Antistin* or *Anthisan* in a dose of 100 mg thrice daily) may be useful Prednisolone is also helpful In cases with acute allergic symptoms antihistaminics may be given by intramuscular or if necessary slow intravenous injection

CELLULITIS AND ABSCESSES Appropriate surgical treatment by incision and drainage along with sulpha drugs and penicillin or penicillin alone

EXTRACTION OF WORM Repeated daily douching of the affected part with sterile cold water promotes the complete expulsion of all embryos and subsequent gentle traction on the protruding part of the worm by a silk thread attached to a match stick will help the extraction of the worm The outline of the subjacent worm becomes clearly visible by spraying the adjacent tissues with ethyl chloride spray

In cases where no ulcer is present and the worm is felt as a convoluted cord under the skin the coils may be injected at several points with a few drops of bichloride of mercury solution (1 in 1000) The killed worm is then excised *en masse* or in parts by several incisions over the palpable segments of the worm under local anæsthesia Fairley and Liston advocate extraction of the worm by operation even in the presence of a blister or an ulcer

PREVENTIVE MEASURES

1 Protection of drinking water in wells and tanks of the endemic areas against guinea worm infection by constructing suitable platforms and fitting pumps for drawing water

2 Addition of potassium permanganate perchloron (bleaching powder substitute) or caustic potash to the water of well or tanks every fortnight

3 Boiling of drinking water or straining it through a piece of coarse cloth before use This method may be easily employed with success for personal prophylaxis

4 Cultivation of barbel fish (*Barbus puckelli*) in the infected wells and tanks This fish feeds both on the cyclops and the larvæ of *D medinensis*

5 Heating of well water to 65°C by portable steam generators at weekly intervals (*Leiper*) It is too costly to be used on a wide scale in India

N V B

A COMPARATIVE TABLE OF DIFFERENT ANTHELMINTIC DRUGS

Drug	Character	Dose		Mode of administration	Main indications	Toxic reactions	Remarks
		Children	Adult				
Bephenium hydroxynaphthoate (*Alcopar*)	Synthetic powder	5 g can be given above 1 year	[illegible] g in one dose or 5 g t d s for 1 day	Mixed with water on empty stomach	Hookworm disease Ascariasis	Only slight nausea	Very safe drug
Carbon tetrachloride	Clear colourless liquid	3 [illegible] for each year of age	3 cm	On empty stomach in the form of emulsion with skimmed milk or liquid paraffin or shaken up with 1 oz saline purgative	Hookworm disease Taeniasis Enterobiasis	Giddiness, drowsiness, toxic hepatic necrosis	Contraindicated in hepatic cirrhosis, severe anaemia, colitis and other duodenal disease
Diphenan	White crystalline available as 0 5 g tablets	Proportionately smaller dose	3 g	In three divided doses 1 hour before meals for 7 days	Enterobiasis	Nausea, vomiting, haemolytic anaemia	Should be used under close supervision
Dithiazanine	Synthetic available as enteric coated tablets	Proportionately smaller dose	100 to 200 mg t d s after food	Usually for 5 days for strongyloidiasis 14—21 days	Enterobiasis Strongyloidiasis Trichuriasis Ascariasis	Sometimes causes nausea, diarrhoea	A new effective drug with broad range of action

A COMPARATIVE TABLE OF DIFFERENT ANTHELMINTIC DRUGS (Contd)

Drug	Character	Dose: Children	Dose: Adult	Mode of administration	Main indications	Toxic reactions	Remarks
Ext Filicis liquidum	Liquid	3 m for each year of age	3 6 c cm	On empty stomach in gelatin capsule or in the form of emulsion Given in 3 divided doses at intervals of ½ hour Saline purgative 1 hour after last dose	Taeniasis	Headache vomiting giddiness jaundice hæmaturia yellow vision or dim vision optic neuritis delirium coma	
Hetrazan	Synthetic available as 50 mg tablets	1 2 mg per kilogram of body weight for each dose		Three times daily after meals for three weeks	Filariasis	Usual symptoms due to drug are mild malaise slight fever anorexia and headache Systemic allergic reactions may occur	Actively remove the microfilariae from peripheral blood
Hexyl resorcinol	Synthetic crystalline available as pills 0 2 g each	Below 6 years 0 4 g 6 to 8 years 0 6 g 8 to 12 years 0 8 g	1 g	Swallowed on empty stomach	Ascariasis Hookworm disease	Almost nontoxic drug	Very effective in ascariasis suitable for weak and debilitated patients
Medicinal gentian violet (crystal violet)	Greenish bronze crystal or powder	¼ gr for each year of age	3 gr	In three divided doses one hour before meals for 7 days Rest for 7 days and again repeated for 7 days Continued therapy for 15 days could be done for prolonged	Enterobiasis Strongyloidiasis	Transient giddiness vomiting abdominal pain headache nausea	Dependable drug in enterobiasis Contraindicated in severe cardiorenal or hepatic diseases

A COMPARATIVE STUDY OF DIFFERENT ANTHELMINTIC DRUGS (Contd.)

Drug	Character	Dose: Children	Dose: Adult	Mode of administration	Main indications	Toxic reactions	Remarks
Mepacrine	Available as yellow tablets 0.1 g each	Proportionately small dose	0.8 1 g	On empty stomach all at a time or two tablets at interval of 10 minutes	Taeniasis *T. saginata* *T. solium* *H. nana*	Sometimes nausea, giddiness and psychotic symptoms may develop	Very good drug for big tapeworm infection
Oil of chenopodium	Colourless or pale yellow liquid	1 m for each year of apparent age	1 c.cm	On empty stomach in gelatin capsule may also be given in two divided doses at half hourly interval	Ascariasis Hookworm disease	Vomiting, headache, giddiness, coma	Useful in mixed infections of hookworm disease and ascariasis contraindicated in hepatic cirrhosis and cardiorenal diseases unsuitable for children and pregnant women
Piperazine tartrate and diphenyl acetate	Available as tablet, syrups and elixirs	Used in doses equivalent to [illegible]0mg of piperazine hexahydrate per kg of body wt		Usually in three divided doses in a day	Enterobiasis —7 to 14 days Ascariasis— 5 days	Practically nil	Palatable form is very suitable for children. For single dose therapy—safest
Santonin	Colourless crystal turning yellow in sunlight	Approximately 1/8th gr for each year of age	3 *gr*	At *bedtime in a* powder form along with sod. bicarbonate	Ascariasis	Headache, vomiting, diarrhoea, haematuria, xanthuria, xanthopsia	Should be used with caution in infants
Tetrachlorethylene	Colourless liquid	4 m for each year of apparent age	4 c.cm	Given on empty stomach early in the morning along with one oz. of saline purgative	Hookworm disease Taeniasis Enterobiasis	Transient burning sensation in the stomach, slight nausea and occasional giddiness	Drug of choice in the treatment of hookworm disease. *Should not be used* where heavy roundworm infection is co-existent

SECTION III DISEASES CAUSED BY BACTERIA

CHAPTER I

TYPHOID AND PARATYPHOID FEVERS

TYPHOID FEVER

[Enteric fever Typhu abdominalis Autumnal fever]

DEFINITION

It is an acute infectious fever caused by the Bacterium typhosum (*Salmonella typhi*) and characterised clinically in typical cases by (1) long continued pyrexia (2) headache and somnolence (3) relative bradycardia (4) moderate enlargement of the spleen (5) abdominal tenderness and discomfort and (6) rose coloured eruption

But it must be emphasised at the very outset that the clinical picture in typhoid fever is extremely variable

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION Typhoid fever has a world wide distribution It is however most prevalent in tropical and subtropical countries

SEASONAL PREVALENCE The disease occurs in the tropics throughout the year though it is more common during the early rains reaching the peak of incidence during the autumn for which it is also called autumnal fever

AGE SEX AND RACE INCIDENCE It is more commonly seen in young adults between 15 to 35 years of age but not at all uncommon in children It is very rare in infants Both sexes are equally liable to the disease The adult population in the tropics is to a great extent immune to the disease as a result of previous infections in childhood Persons newly arrived in the tropics are most susceptible to infection if they are not previously protected against it by inoculation Protective inoculations have reduced the incidence of the disease at present

IMMUNITY One attack usually confers protection for life but second and even third attacks have been seen to occur

CAUSATIVE ORGANISM The organism of typhoid fever is Bacterium typhosum (*Salmonella typhi*) which was first observed by Eberth in the mesenteric glands intestinal ulcers and spleen of autopsy

cases of typhoid fever and described by him in 1880 It is an actively motile flagellated rod shaped gram negative organism about 3 *microns* in length and 0 5 *micron* in breadth which is recognised by the characteristic biochemical and specific serological reactions It may survive for a long time in water and even in ice and it multiplies freely in milk and butter Its optimum growth is seen at blood heat It is quickly killed by boiling water and within 15 minutes when exposed to a temperature of 60°C The toxins are mainly intracellular

MODE OF INFECTION

Bact typhosum usually gains entrance to the body of the host through contaminated food or drink Such a contamination may occur by one of the following agents

1 CARRIERS There are three types of carriers

(*a*) *Acute or Convalescent Carriers* They are convalescent typhoid patients excreting typhoid bacilli in their fæces and other discharges for a variable period during convalescence

(*b*) *Chronic Carriers* They are patients who recover from typhoid fever but continue to harbour and discharge the germs in their excreta for years (5 per cent of cases) Usually the gall bladder the intestinal tract and occasionally the renal pelvis are the seats of infection in such cases Intestinal carriers are much more common than urinary carriers Occasionally however the reticulo endothelium of the bone marrow may form an important depot for the typhoid organisms for months after convalescence

Chronic carriers employed in kitchens dairy or bakery as cooks or servants or entrusted with the distribution of food or drink prove to be an important source of infection

(*c*) *Contact or Apparently Healthy Carriers* They are persons who give no history of any previous attack of typhoid fever and still pass the bacilli in their stools or urine

2 WATER SUPPLY The drinking water in cities may be contaminated by sewage and in rural areas may be polluted by the washing of infected clothes and linens in tanks and rivers This is the usual cause of large epidemics

3 FLIES In the tropics the flies are very active agents in the spread of the disease by alternately visiting and feeding on infected fæcal matter and on food

4 FOMITES Occasionally a direct infection may occur from

contact with the patient or from handling the articles used by the patient, such as the feeding cups douching tubes the bed pans soiled linen etc.

PATHOLOGY

On escaping the destructive action of the antiseptic acid barrier of the stomach under conditions of low gastric acidity the bacilli reach the small intestine multiply in its alkaline medium and invade the lymphoid tissues of the Peyer s patches and the solitary lymph follicles from which they pass into the blood stream *via* the mesenteric lymph nodes and the thoracic duct and cause a bacteriæmia Some of the bacilli entering the circulation are destroyed with liberation of their endotoxins which cause the fever Others settle down in the lymphoid tissues of the small *intestine mesenteric* lymph nodes spleen liver and bone marrow The rest are excreted in stools bile urine vomit and purulent discharges of the patients which directly or indirectly may act as potent sources of infection

INTESTINAL LESIONS The characteristic lesions which are found mainly in the Peyer s patches and the solitary lymph follicles of the *small intestine may be described in the following stage*

1 *Stage of Hyperæmia and Swelling* The endotoxins liberated by the disintegration of some of the bacilli produce intense hyperæmia and hyperplasia of the lymphoid tissues and proliferation of the large mononuclear cells of the reticulo-endothelial system in the early stage of the disease Hence they appear reddish grey in colour swollen and *raised above the surrounding surface This condition reaches its* height from the 8th to 10th day of the illness After the 10th day in a mild and favourable case of typhoid fever the swelling and hyperæmia of the Peyer s patches and the isolated lymph follicles go on decreasing till the 14th day and by the end of the third week the resolution is almost complete

2 *Stage of Necrosis and Slough Formation* In a moderately severe case in the second week greyish areas of necrosis appear in the inflamed lymphoid structures and yellowish brown sloughs are formed The necrosis is due to the blockage of the minute vessels by the proliferated mononuclear cells and also due to a direct action of the bacillary toxins

3 *Stage of Ulceration* The sloughs separate in the third and early part of the fourth week and give rise to multiple ulcers During separation of the sloughs hæmorrhage may occur due to erosion of bloodvessels perforation and peritonitis may also result if the ulcer extends too deeply The ulcers have got certain characteristic features

They are situated in the long axis of the bowel opposite the mesenteric attachment and are most abundant within the last one or two feet of the ileum and more confluent near the ileo cæcal valve where the lymphoid structures are numerous The cæcum and the proximal part of the colon may be involved in one third of the cases The stomach duodenum and first part of the jejunum are involved only in rare instances The ulcers involving the Peyer s patches are ovoid whereas those involving the solitary lymph follicles are usually round Their edges are raised and moderately undermined and the floor is either worm eaten in appearance or smooth being formed by the muscular or even the peritoneal coat It is essential to bear in mind that the extent and severity of the intestinal ulcers bear no constant relation to the intensity of the clinical signs and symptoms There are cases where the patients die of typhoid fever without showing any actual ulcer of the intestine at autopsy

4 *Stage of Healing* Towards the middle of the fourth week the ulcers begin to heal with complete restoration of the mucous membrane and formation of little or no scar tissue Hence unlike tuberculous ulcers intestinal stricture is never a sequel of typhoid ulceration The process of healing is not however complete in all the ulcers at the same time There is a slaty pigmentation with slight depression at the site of healed ulcers

Mesenteric Lymph Nodes They are hyperæmic and swollen due to proliferation of the large mononuclear cells The glands draining the lower part of the ileum are specially involved By the 9th day they may be as large as a hen s egg dark in colour soft and pulpy Suppuration and rupture of the glands are very rare

Spleen It is soft dark red in colour and moderately enlarged in the early stage due to marked hyperæmia and hyperplasia of the lymphoid and the phagocytic mononuclear cells blocking the splenic veins Necrotic areas are frequently seen The spleen returns to its normal size about the fourth week In rare cases rupture of the spleen may occur spontaneously or due to trauma

Liver Areas of focal necrosis and of accumulated mononuclear cells are found scattered in the liver parenchyma the cells of which show in addition varying degrees of cloudy swelling Hepatic abscess and pyelophlebitis are very rare

Gall bladder The gall bladder is frequently infected in typhoid fever and cholecystitis may result either in the course of typhoid fever

or afterwards The cholecystitis is usually catarrhal but it may be suppurative

RESPIRATORY ORGANS The lungs very often show evidence of bronchitis and bronchopneumonic consolidation Lobar pneumonia may occur in some cases Hypostatic congestion of the lung is common Fibrinous sero fibrinous or even purulent pleurisy are occasionally met with Abscesses and gangrene are definitely rare Ulceration of the larynx may occur rarely

HEART AND BLOOD VESSELS Heart usually shows cloudy swelling fatty and granular degeneration of the myocardium Pericarditis and endocarditis are rare Thrombosis of the femoral and saphenous vein specially on the left side is not uncommon

BRAIN AND MENINGES Typhoid meningitis is very rare Meningism is quite common Hyperæmia and œdema of the brain may however occur in one third of the cases (*Hoffmann*)

KIDNEYS A cloudy swelling of the renal parenchyma is usually found Acute diffuse nephritis is rare Pyelonephritis and cystitis due to Bact typhosum or sometimes due to *Esch coli* are rather frequent

VOLUNTARY MUSCLES Zenker s hyaline degeneration of the muscles though not confined to typhoid fever alone is commonly seen in this disease It is found in the rectus abdominis adductors of the thigh and the diaphragm There may be rupture of the affected muscles with hæmorrhage

BONES Osteoperiostitis and osteomyelitis of the tibia lower end of the radius clavicle rib and vertebra may occur in course of the acute illness Chronic abscess es of the bone may occur months or years after recovery from typhoid fever

CLINICAL MANIFESTATIONS

INCUBATION PERIOD Usually it is 10 15 days though it may vary from 5 to 45 days

MODE OF ONSET The onset is usually insidious without any localising sign or symptom In children and in some of the adults a sudden onset is not uncommon Prodromal symptoms are often few The common premonitory symptoms are frontal headache lassitude anorexia mild bronchitis sore throat vague abdominal discomfort constipation or diarrhœa chilly sensations muscular pains and epistaxis The clinical features of a typical case of typhoid fever may conveniently be described from week to week as follows

FIRST WEEK *General Appearance* The patient is somewhat listless and lethargic lying usually on his back The cheeks are flushed and the eyes bright

Fever The temperature rises steadily by steps (ladder like rise) being a degree or more higher on each successive day or night (Fig 30)

Alimentary System The tongue is coated with a whitish fur in the middle the tip and the margins are red and clear Anorexia is present Nausea and vomiting though rare have been observed by Banerjea in a few cases Abdomen is tumid and slightly tender Gurgling in the right iliac fossa may be present but it is neither a constant nor an important sign The bowels are usually constipated but may be loose

Spleen is palpable in 75 per cent of cases towards the end of the first week between 6th and 8th days It is soft and inspite of the enlargement it may not be always palpable

Liver is palpable in about 50 per cent cases by the end of the first week

Circulatory System The pulse is slow in proportion to the height of the temperature and is often dicrotic due to the relaxation of the peripheral arterial tone Heart sounds do not show any abnormality except in severely toxic and septicæmic cases

Respiratory System Usually there are signs of mild bronchitis associated with slight cough occasionally signs of pneumonia may be present In children it is not uncommon to find evidences of bronchopneumonia

Nervous System Headache is frequently present at the onset but it diminishes towards the beginning of the second week There is mental apathy which gradually passes into stupor with the progress of toxæmia In septicæmic cases a wild delirium is occasionally seen

Urinary System The urine is high coloured with a high specific gravity as in other febrile diseases occasionally showing a trace of albumin and hyaline casts

Skin Rose spots appear in successive crops over the abdomen the sides of the chest and the back between 7th and 10th days They are lightly elevated circular pinkish papules 2 to 3 mm in diameter usually a few in number and disappear on pressure Each spot lasts for 3-4 days and gradually fades away leaving a faint brownish tint In some cases such spots are seen to appear from the 19th to the 34th day They are distributed over the buttocks thighs

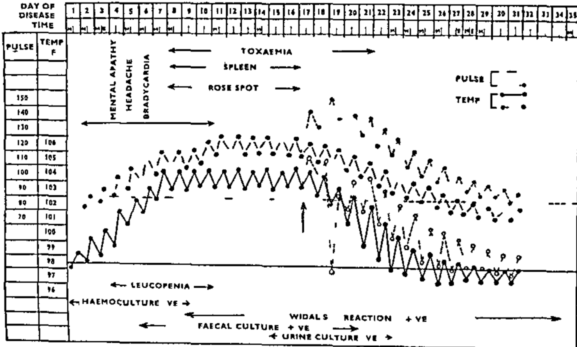


Fig 30 Slowing temperature chart of typhoid fever The interrupted lines indicate pulse and temperature variations in a case of typhoid fever complicated with intestinal haemorrhage

forearms arms and even the face in hundreds simulating a measly ra h The rose spots are due to bacterial embolus with focal accumulation of mononuclear cells around dilated capillaries in the sl in and Bact typhosum may be recovered from them

The rash has been observed by Banerjea in 45 per cent of the cases of typhoid fever amongst the Indians in Calcutta

Laboratory Findings The leucocyte count is often normal or slightly high (8 000 10 000 per c mm) with a slight increase of poly morphonuclear cells and absence of eosinophil

SECOND WEEK With the advent of the second week the clini al picture is rather characteristic depending upon the severity of the associated toxæmia The patient is stuporo e and does not properly respond to questions

Fe er The temperature reaches its fastigium and becomes steady varying between 103°F (Fig 30)

Alimentary System The tongue is coated with a yellowish white fur at the centre the margins and the tip are red The lips teeth and gums may be dry and covered with sordes which consist of a mixture of food micro organisms and epithelial debris The abdomen gets more tumid and tympanites appears as a result of the toxic paresis of the intestinal musculature The bowels may be loose several liquid motions like pea soup may be passed in 24 hours but more commonly there is constipation

Spleen is larger and more definitely palpable It is soft In some cases it is enlarged upto 2 3 fingers breadth below costal margin

Circulatory System The pulse may still be slow but dicrotism disappears More commonly however the pul e is soft and rapid (120 to 140 per minute) Heart sounds are feebler There may be a gallop or a fœtal rhythm A soft systolic murmur may appear over the apical area The bloodpressure falls gradually and the sy tolic pressure may be as low as 80 mm of Hg

R spiratory System Respiration may be hurried with evidence of bronchopneumonic patches in the lungs Hypostatic congestion of the lung bases is frequently present

Two important events may occur towards the end of this second week viz hæmorrhage from the bowels and perforation

Laboratory Findings The blood usually shows moderate anæmia with granulopenia and relative increase of lymphocytes and monocytes The leucopenia may be as low as 1 000 per c.mm in some cases Leucocytosis 10 000 15 000 per c.mm may occur in the presence of complica

tions such as bronchopneumonia urinary infection severe diarrhœa intestinal hæmorrhage and perforative peritonitis The writer has noted a leucocytosis of 25 000 per c mm with a polymorphonuclear cell count of 90 per cent in a case complicated with pyelonephritis

THIRD WEEK In mild cases the symptoms may not increase The temperature begins to remit and tends to decline gradually (*lysis*) towards the end of this week

In severe and neglected cases however the patient passes into a *typhoid state* (not confined to typhoid fever alone) characterized by

(*a*) coma with low muttering delirium

(*b*) marked muscular prostration and helpless dorsal decubitus with inability to turn on the sides and tending to sink into the centre of the bed

(*c*) wide open eyes (*coma vigil*) slight dilatation of pupils and dull expression

(*d*) tremors of the fingers and twitching of the muscular tendons (*subsultus tendinum*)

(*e*) picking at the bed clothes (*carphologia*) the nose and lips

(*f*) dry tremulous tongue coated with a thick brown fur the tip and edges looking red and raw and protruded out with difficulty

(*g*) dry lips gums and teeth covered with sordes

(*h*) occasionally bleeding from gums

(*i*) involuntary passage of urine and fæces or retention of urine

The temperature remains steady at 104° or 105°F or may rise higher The pulse is very feeble and as rapid as 140 165 per minute and sometimes even more It may be irregular due to occurrence of extrasystoles or rarely auricular fibrillation and heart block The hands and feet may be cold and livid The apical first sound is very weak The lungs may show evidences of bronchopneumonia or lobar pneumonia The larynx may show ulceration in a few cases with hoarseness of the voice and dysphagia Tympanites is marked Hæmorrhage from the bowels and perforation may supervene A secondary invasion of the blood stream by hæmolytic streptococci through the intestinal ulcers has never been observed by us A secondary infection of the urinary tract due to *Esch coli* may occur

FOURTH WEEK In severe cases there is aggravation of all the signs and symptoms described above In uncomplicated cases steadily convalescence begins temperature comes down to normal or may be subnormal The tongue becomes gradually clean and appetite returns Spleen returns to its normal size and is no longer palpable The pulse

however remains rapid and unduly excitable Heart sounds are still feeble

FIFTH AND SIXTH WEEKS In favourable cases the patient steadily progresses towards recovery In severe cases the patient may still be in the same condition as in the second and third weeks marked toxæmia may persist hæmorrhage and perforation may rarely occur and cause a fatal termination The long continued cases are however not necessarily fatal though they may cause extreme anxiety

Typhoid fever may show wide variations from the typical clinical picture in its mode of onset and course It also shows certain important variations from the adult type when it occurs in children the aged and the pregnant women

ATYPICAL MODES OF ONSET 1 Sudden onset with chill or rigor

2 With symptoms of lobar pneumonia (*pneumo typhoid*) or acute pleurisy (*pleuro typhoid*) With laryngeal symptoms such as hoarseness or aphonia

3 With signs and symptoms of meningism such as severe headache photophobia rigidity of the muscles of neck and back twitching of muscles and convulsions (*meningo typhoid*)

4 With signs and symptoms of gastro intestinal disturbances (*a*) Symptoms of acute gastritis—nausea and vomiting (*b*) Symptoms of acute appendicitis—pain in the right iliac fossa without any definite rigidity of the abdomen (*c*) Diarrhœa

5 With signs and symptoms of localised infection in (*a*) the urinary bladder—cystitis (*b*) the liver—hepatitis and (*c*) the gall bladder—cholecystitis

6 With hæmaturia due to acute focal nephritis (*nephro typhoid*)

7 With hæmorrhagic symptoms characterised by hæmorrhages from the various mucous membranes and into the skin muscles brain and meninges

ATYPICAL VARIATIONS IN COURSE 1 *Abortive Form* The fever is light or ends by lysis about the second week or earlier

2 *Ambulatory Form* In one group of cases the patient is not ill enough to take to bed and carries on his work He comes under observation in the second week with severe signs and symptoms such as acute delirium circulatory failure intestinal hæmorrhage or perforation In another group of cases the fever is mild and the constitutional disturbances are slight throughout the illness

3 *Afebrile Form* It is extremely rare and is said to occur in markedly debilitated persons

TYPHOID FEVER IN CHILDHOOD (1) *Sudden onset with vomiting and diarrhœa* (2) Presence of meningism at onset (3) The temperature is remittent or intermittent (4) The course is usually prolonged to 5-6 weeks (5) Bronchopneumonia is a common complication (6) Ketonæmia is rather common (7) Hæmorrhage and perforation are rare because the intestinal lesions are less marked than in adults and the ulceration of the solitary lymph follicles and Peyer's patches is uncommon However hæmorrhage in an infant of eleven months with recovery and hæmorrhage and perforation in a girl of three years ending fatally have been seen (*Banerjea*) (8) Mortality is less than in adults

TYPHOID FEVER IN THE AGED (1) Rare occurrence (2) Fever is slight and irregular or even absent (3) Complications such as hypostatic pneumonia and heart failure are common (4) Mortality is very high (5) Convalescence is often prolonged in cases that recover

TYPHOID FEVER WITH PREGNANCY Abortion or premature delivery occurs in 60 per cent of cases

COMPLICATIONS

DIGESTIVE SYSTEM If the mouth is not kept properly clean in severe and toxic cases inflammation may spread along Stensen's duct to the parotid gland and give rise usually in the third week to a suppurative *parotitis* on one or either sides It is however a rare complication Occasionally superficial ulcers (*Duguet's ulcers*) may develop towards the end of the first week on the anterior pillars of the fauces the soft palate and on the pharyngeal wall Such ulceration occurs in about 1 per cent of typhoid fever cases and if this fact is not kept in mind a wrong diagnosis of diphtheria may be made specially in children Marked *tympanites* which is due to a toxic paresis of the intestine or stomach is a frequent and very troublesome complication interfering with the efficient action of the heart and æration of the lower lobes of the lungs It may also set up specially in children a reflex bronchiolar spasm and lead to lung complications such as *bronchopneumonia* or collapse Persistent *diarrhœa* is often seen towards the end of the second week or the beginning of the third week and it may herald the onset of a severe complication such as hæmorrhage from the bowel or perforation

Intestinal *hæmorrhage* occurs in 5 to 7 per cent of cases of typhoid fever towards the end of second week or in the third or fourth week

due to erosion of a vessel during separation of sloughs It is rare in children below the age of 8 years It may be slight moderate or severe If the blood is copious and expelled from the bowels quickly it appears as a bright red liquid but if small and retained in the bowels for some time it appears as dark red clots The signs and symptoms of hæmorrhage depend on its amount In a severe hæmorrhage there is a sudden drop in the temperature to the normal or more commonly subnormal level with a small rapid pulse (Fig 30) and shallow quick respiration The patient is pale restless and often delirious The extremities are cold and the bloodpressure falls to 90 or 80 mm of Hg The hæmorrhage may be single or it may be repeated for a few days The mortality of cases of intestinal hæmorrhage which varies from 20 to 50 per cent is influenced by the amount of blood loss the degree of associated toxæmia and the nutrition of the patient The writer has seen cases where inspite of repeated hæmorrhages the patient was tided over to fall a prey to cardiac failure due to subsequent toxæmia

Perforation of the bowels occurs in 2 to 4 per cent of cases usually in the third week and not uncommonly in the fourth or even the fifth week It is rare in young children Both hæmorrhage and perforation are likely to occur in severe cases of typhoid fever with marked tympanites and persistent diarrhœa Perforation may or may not be preceded by hæmorrhage The sites of perforation in order of frequency are lower part of ileum (within 12 inches of the ileocæcal valve) cæcum appendix colon jejunum and sigmoid (*Meakins*) The perforation is usually single rarely several The onset of perforation is heralded by a sudden severe abdominal pain referred at first to the right iliac fossa and later spreading all over the abdomen The patient is in a condition of shock with pinched facies a sudden drop of the temperature to subnormal and rapid pulse and respiration In some cases the temperature may not be affected and in others it may rise Abdominal movement is diminished specially over the right iliac fossa or the hypogastric region and rectal tenderness is present Obliteration of the liver dulness in the midaxillary line and dulness in the flanks are helpful signs Symptoms and signs of *general peritonitis* develop after the lapse of a few hours The temperature rises and a rising leucocyte count with increase of neutrophils is often found on hourly examination It must be remembered that in some cases the clinical picture described above may be absent and the diagnosis becomes extremely difficult

Non perforative peritonitis may rarely occur due to a spread of the infection through the intestinal wall

LIVER AND GALL BLADDER Acute *cholecystitis* may sometimes occur as a complication in the first week of typhoid fever and give rise to difficulties in diagnosis A few cases of this nature have been seen by the writer *Acute cholangitis jaundice perforation of the gall bladder* and *abscess of the liver* are very rare

SPLEEN *Splenic abscess* and *spontaneous rupture* of the spleen have been reported in rare cases

RESPIRATORY SYSTEM *Bronchitis* of varying degrees is present in almost all cases In severe cases and in feeble patients *hypostatic congestion* of the lungs due to prolonged recumbent position is not uncommon in the second or third week *Lobar pneumonia* and *bronchopneumonia* may occur about the same period They are usually caused by secondary infections with *D pneumoniæ* or hæmolytic streptococci and not with Bact typhosum though it may be present in the sputum *Fibrinous pleurisy* or *pleural effusion* may occur in some cases in association with the pneumonic process *Empyema lung abscess infarcts* and *spontaneous pneumothorax* are rare

CIRCULATORY SYSTEM *Acute myocardial* or *peripheral failure* is a common complication in severe cases *Pericarditis* and *endocarditis* are very rare *Venous thrombosis* is not uncommon during the third or fourth week when convalescence has set in It frequently affects the left femoral vein which feels like a cord and is tender The left leg is swollen distal to the site of thrombosis *Arteritis arterial thrombosis* and *gangrene* are rare

NERVOUS SYSTEM *Meningism* may occur at onset or sometimes later in course of the fever specially in children Marked headache photophobia rigidity of the neck muscles Kernig's sign muscular twitchings and occasionally convulsions associated with meningism are not due to any inflammatory changes in the meninges or the brain and spinal cord but due to congestion and in some cases in the tropics due to the associated presence of a heavy ascaris infection

True typhoid *meningitis* with a turbid or purulent cerebrospinal fluid yielding a pure culture of Bact typhosum may occur late in the disease but is definitely rare The occurrence of a low muttering delirium with coma vigil subsultus tendinum and carphologia is rather common in the late stages of severely toxic cases Violent delirium is rare and if present indicates the supervention of *meningitis* or *encephalitis* *Delirium tremens* may develop in alcoholic subjects

Convulsions are rare When they occur the usual cause is

meningi m Rare causes are *encephalitis cerebral thrombosis and meningitis*

H miplegia anl *aphasia* may rarely occur in course of the fever

Mental disturbances such as *mania m lancholia* or *dementia* may occasionally develop at the height of the illness or during convalescence Complete recovery occurs in course of a year or two

Myelitis and an *acut form of as nding paralysis (Landry s typ)* may occasionally occur

P riph ral neuritis may appear late in the disease or during con valescence The nerves of the lower extremities are often involved Tenderness of the toes during convalescence is probably due to neuriti

SPECIAL SENSES *Ey Conjuncti itis iritis opti neuritis* and *r tinal hæmorrhag* are rare

Ear Temporary deafness is a common symptom in course of the disease *Otitis media* is rare

URINARY SYSTEM *Acut hæmorrhagic nephritis* may occur at onset or sometimes late and is very rare *Cystitis py litis* or *pyelo n phritis* are not uncommon complications during the third week and they are caused either by Bact typhosum or by *Esch coli* Typhoid bacilluria is rather common

GENERATIVE SYSTEM *Orchitis prostatitis* and *o aritis* are rare

LOCOMOTOR SYSTEM *P riostitis* and *abscess* of the ribs clavicle or long bones such as tibia or femur may develop during convalescence or many months after an attack of typhoid fever

Arthritis of one or more large joints frequently of the hip or knee joint may occur and lead to a spontaneous dislocation

Typhoid spine associated with pain on movement in the dorso lumbar region of the spine and rigidity of the spinal muscles is due to an inflammatory process involving the vertebræ and perivertebral structures In some cases the symptoms are purely neurotic manifesta tion It is a rare complication during convalescence

Rupture of muscles such as rectus abdominis or adductors of the thigh with localised hæmorrhage may rarely occur

SKIN *Sudaminal* eruptions are found in many cases over the abdomen and in the axillæ The appearance of sudamina is regarded to be of good prognostic significance

B d sores They are complications in severe ca es where proper

nursing and care of the skin are lacking Such sores occur over pressure points *as* sacral regions and heels and may cause septicæmia due to secondary infections

Abscesses and boils These may develop late in the disease or during convalescence

Besides those already mentioned *hyperpyrexia* is sometimes met with in severely toxæmic cases

COMMON COMPLICATIONS

The following complications which we have commonly met with are enumerated in order of frequency

(1) Tympanites (2) Diarrhœa (3) Marked bronchitis broncho-pneumonia or hypostatic pneumonia (4) Acute circulatory failure (5) Coma with low muttering delirium (6) Infection of the urinary tract (7) Hæmorrhage from the bowels (8) Bed sores (9) Parotitis (10) Perforation and peritonitis

SEQUELÆ

1 Relapse It is a second attack of typhoid fever which occurs in 10 15 per cent cases after an afebrile period of 8 15 days All the signs and symptoms characteristic of typhoid fever appear again As a rule a relapse is milder than the original attack and the course is about 1 2 weeks In some cases however it may be more severe than the primary attack and prove fatal Relapses are more common in children and in cases where the primary attack is mild It is rare to have more than one relapse though two relapses in a child of eight have been noted (*Banerjea*) and as many as 5 relapses have been recorded by David The cause of relapse is not definitely known The most probable explanation is re invasion of the blood by typhoid bacilli which were lying inactive in such reservoirs as the gall bladder or the bone marrow and their subsequent localisation in the intestine

2 Leishmanial infection A secondary attack of fever during convalescence from typhoid fever is not necessarily due to a relapse but it may be due to an acute kala azar supervening on typhoid fever or manifesting itself with a typhoid like onset and hence missed during the primary attack

3 Infections of the urinary tract with *Esch coli* or occasionally with typhoid bacilli

4 Chronic cholecystitis and cholelithiasis

5 Femoral thrombosis

6 Aphasia and deafness Both these sequelæ are temporary and rather common in children Recovery occurs in a few weeks

7 Post typhoid psychoses *e g* mania melancholia or dementia Recovery occurs in six to twelve months Post typhoid neurasthenia —may last for months or years

8 Chronic periostitis of the long bones and ribs bone absce ses osteomyelitis typhoid spine

9 Peripheral neuritis

10 Baldness in children but temporary

11 Subcutaneous abscesses—developing months after convalescence the pus shows on culture Bact typhosum

12 Contractures deformities

DIAGNOSIS

In typical cases of typhoid fever the diagnosis is not difficult But as already mentioned variations from the usual type are not uncommon and in such cases the diagnosis baffles the most experienced observer The laboratory also may fail to throw light in some such cases Hence we would emphasize that in view of the wide prevalence of typhoid fever in the tropics *every case of remittent or continued fever lasting for more than 5 6 days and showing no signs of localisation should be suspected as typhoid fever until it is proved otherwise*

A critical study of all available clinical data is essential for an early diagnosis without which an efficient management of the patient and the early adoption of preventive measures are not possible

The laboratory data are undoubtedly of great importance in obscure cases and they serve to confirm the diagno is in others

Thus typhoid fever may be diagnosed accurately in most cases on a correlation of the following data

CLINICAL DATA 1 Remittent fever with a ladder like a cent of temperature in the first week continuous pyrexia in the second and third weeks ending by lysis in the fourth or fifth week

2 Relative bradycardia and presence of dicrotism

3 Headache mental apathy and stupor

4 Mild bronchitis

5 The characteristic tongue with white h fur on the dorsum the margins and the tip looking clean and red

6 Tumid abdomen with tenderness

7 Presence of a soft slightly palpable spleen from the sixth to eight day of fever

8 Roseolar rash

LABORATORY DATA 1 *Blood Examination* Moderate leucopenia with relative lymphocytosis diminution of polymorphs and absence of eosinophils

2 *Cultural Methods* (*a*) Blood culture In the first week of typhoid fever it yields positive results in 95 per cent cases in the 2nd week in 70 per cent in the 3rd week in 45 per cent and in the 4th week 40 per cent It is thus an extremely valuable method of an early diagnosis of typhoid fever where facilities exist and a positive hæmoculture is a conclusive evidence of typhoid fever

(*b*) Clot culture is said to be superior to blood culture

(*c*) Cultures of stool and urine Positive results are usually obtained during the 1st to 4th week of typhoid fever Catheter specimen of urine shows Bact typhosum in 25 per cent of cases between 3rd and 4th weeks The excretion of the bacilli in urine is intermittent in nature due to transient bacilluria

(*d*) Culture of the sternal puncture material may yield positive results in late stages or in convalescence even when cultures of blood fæces and urine are negative

3 *Widal s test* The Widal s test is usually positive in most cases after the 8th or 9th day of typhoid fever though a few positive results have been seen (*Banerjea*) as early as the 5th day This is a specific test and it depends on the appearance in the blood of typhoid patients of two types of agglutinins somatic O and flagellar H corresponding to O and H antigens in typhoid bacilli More recently Felix has demonstrated a third antigen called Vi which is associated with virulence The O agglutinin appears earlier than H agglutinin though it may not be demonstrable till the third week or later but the latter agglutinin reaches *a much higher titre in the serum than the former* The H agglutinin is a specific response whereas the O agglutinin is a common response to the enteric group of infections In a few cases of typhoid fever due to infection with a nonmotile strain of Bact typhosum H agglutinins may never appear though O agglutinins appear in the serum H agglutination in a titre of 1 in 50 or over in the serum of a patient suffering from fever is not always diagnostic of typhoid fever It may be the result of previous inoculation with T A B vaccine or of a previous attack of typhoid fever Even a rising titre of H agglutinin may be obtained in such cases (*anamnestic reaction*) in response to an infection with organisms other than Bact typhosum Here the presence of O agglutinin however in a titre of 1 in 100 or more is an indication of enteric infection

Hence it is essential that Widal's test both for H and O agglutinins should be done more than once and a rising titre of both agglutinins is diagnostic of typhoid fever. Cases of typhoid fever where there is no progressive rise in the titre of O agglutinin seem to have a bad prognosis. Demonstration of Vi antibody (by an agglutination test on typhoid cultures containing the Vi antigen as described by Felix) is often possible early in the 1st week of the disease and is conclusive proof of quite recent or existing typhoid infection even when detectable in small amount. The reaction is, however, also positive in chronic typhoid carriers and in rare cases of paratyphoid fever of the C type.

DIFFERENTIAL DIAGNOSIS

On account of its variable clinical course, occasional anomalous features and marked localisation of infection at the onset in various organs, typhoid fever may simulate a large number of diseases which cause great difficulties in diagnosis.

The following important diseases can be differentiated from typhoid fever by the characteristic features mentioned against each.

1. MALIGNANT TERTIAN MALARIA. (a) Sudden onset. (b) Early appearance of one or more of the following symptoms, e.g., chill, rigor, delirium, coma, convulsions, bilious vomiting, diarrhœa, pallor and icteric tinge of the conjunctivæ. (c) Unduly rapid pulse, though a relative bradycardia is not uncommon. (d) Wide diurnal variations in the temperature. (e) An early splenic and hepatic enlargement. (f) Presence of malaria parasites in the blood smear. (g) Response to antimalarial drugs.

2. ACUTE KALA AZAR. (a) Presence of double rise in the temperature. (b) Absence of toxæmia. (c) Presence of a clean tongue and a good appetite. (d) Progressive enlargement of the spleen and liver. (e) Progressive leucopenia with diminution of the polymorphs and relative increase of lymphocytes. (f) Positive Complement Fixation test and Chopra's test. (g) Positive flagellate culture.

3. PARATYPHOID FEVERS. (a) Onset with acute symptoms of gastro-intestinal disturbance fairly common, e.g., nausea, vomiting, epigastric pain, diarrhœa, abdominal discomfort, etc. (b) Toxæmia usually slight or absent. (c) Rarity of intestinal complications such as marked abdominal distension, hæmorrhage or perforation. (d) Positive blood culture and agglutination test to *S. paratyphi A* or *B*.

4. PNEUMONIA AND BRONCHOPNEUMONIA. (a) Flushed and rest

LABORATORY DATA 1 *Blood Examination* Moderate leucopenia with relative lymphocytosis diminution of polymorphs and absence of eosinophils

2 *Cultural Methods* (*a*) Blood culture In the first week of typhoid fever it yields positive results in 95 per cent cases in the 2nd week in 70 per cent in the 3rd week in 45 per cent and in the 4th week 40 per cent It is thus an extremely valuable method of an early diagnosis of typhoid fever where facilities exist and a positive hæmoculture is a conclusive evidence of typhoid fever

(*b*) Clot culture is said to be superior to blood culture

(*c*) Cultures of stool and urine Positive results are usually obtained during the 1st to 4th week of typhoid fever Catheter specimen of urine shows Bact typhosum in 25 per cent of cases between 3rd and 4th weeks The excretion of the bacilli in urine is intermittent in nature due to transient bacilluria

(*d*) Culture of the sternal puncture material may yield positive results in late stages or in convalescence even when cultures of blood fæces and urine are negative

3 *Widal s test* The Widal s test is usually positive in most cases after the 8th or 9th day of typhoid fever though a few positive results have been seen (*Banerjea*) as early as the 5th day This is a specific test and it depends on the appearance in the blood of typhoid patients of two types of agglutinins somatic O and flagellar H corresponding to O and H antigens in typhoid bacilli More recently Felix has demonstrated a third antigen called Vi which is associated with virulence The O agglutinin appears earlier than H agglutinin though it may not be demonstrable till the third week or later but the latter agglutinin reaches a much higher titre in the serum than the former The H agglutinin is a specific response whereas the O agglutinin is a common response to the enteric group of infections In a few cases of typhoid fever due to infection with a nonmotile strain of Bact typhosum H agglutinins may never appear though O agglutinins appear in the serum H agglutination in a titre of 1 in 50 or over in the serum of a patient suffering from fever is not always diagnostic of typhoid fever It may be the result of previous inoculation with T A B vaccine or of a previous attack of typhoid fever Even a rising titre of H agglutinin may be obtained in such cases (*anamnestic reaction*) in response to an infection with organisms other than Bact typhosum Here the presence of O agglutinin however in a titre of 1 in 100 or more is an indication of enteric infection

Hence it is essential that Widal's test both for H and O agglutinins should be done more than once and a rising titre of both agglutinins is diagnostic of typhoid fever Cases of typhoid fever where there is no progressive rise in the titre of O agglutinin seem to have a bad prognosis Demonstration of Vi antibody (by an agglutination test on typhoid cultures containing the Vi antigen as described by Felix) is often possibl early in the 1st week of the disease and is conclusive proof of quite recent or existing typhoid infection even when detectable in small amounts The reaction is however also positive in chronic typhoid carriers and in rare cases of paratyphoid fever of the C type

DIFFERENTIAL DIAGNOSIS

On account of its variabl clinical course occasional anomalou features and marked localisation of infection at the onset in variou organs typhoid fever may simulate a large number of disea e which cause great difficulties in diagnosis

The following important diseases can be differentiated from typhoid fever by the characteristic features mentioned against each

1 Malignant Tertian Malaria (*a*) Sudden onset (*b*) Early appearance of one or more of the following symptoms *e g* chill rigor delirium coma convulsions bilious vomiting diarrhœa pallor and icteric tinge of the conjunctivæ (*c*) Unduly rapid pulse though a relative bradycardia is not uncommon (*d*) Wide diurnal variations in the temperature (*e*) An early splenic and hepatic enlargement (*f*) Presence of malaria para ites in the blood smear (*g*) Response to antimalarial drugs

2 Acute Kala azar (*a*) Presence of double rise in the tem perature (*b*) Absence of toxæmia (*c*) Presence of a clean tongue and a good appetite (*d*) Progressive enlargement of the pleen and liver (*e*) Progressive leucopenia with diminution of the polymorphs and relative increa e of lymphocytes (*f*) Positive Complement Fixation test and Chopra s test (*g*) Positive flagellate culture

3 Paratyphoid Fevers (*a*) Onset with acute symptoms of gastro intestinal disturbance fairly common *e g* nausea vomiting epigastric pain diarrhœa abdominal discomfort etc (*b*) Toxæmia usually slight or absent (*c*) Rarity of intestinal complications such as marked abdominal distension hæmorrhage or perforation (*d*) Positive blood culture and agglutination test to *S paratyphi A* or *B*

4 Pneumonia and Bronchopneumonia (*a*) Flushed and rest

less appearance (*b*) Rapid and shallow respiration with inspiratory dilatation of the alæ nasi (*c*) Characteristic lung signs (*d*) Leucocytosis with increase of neutrophils

5 INFLUENZA (*a*) Sudden onset with severe headache (*b*) Pain in the limbs and back (*c*) Presence of oculo nasopharyngeal catarrh (*d*) Short course of about a week in uncomplicated case

6 CEREBROSPINAL MENINGITIS (*a*) Sudden onset (*b*) Persistent headache (*c*) Signs of meningeal irritation (*d*) Lateral decubitus with head retraction (*e*) Leucocytosis (*f*) Turbid or purulent cerebrospinal fluid showing increase of protein and polymorphonuclear cells diminution of glucose and presence of *N meningitidis* in the smear from centrifugalised deposit and on culture

7 ESCH COLI INFECTION OF THE URINARY TRACT (See page 66)

8 ACUTE MILIARY TUBERCULOSIS (*a*) Irregular temperature (*b*) Presence of sweating (*c*) Unduly rapid pulse (*d*) Presence of dyspnœa and cyanosis out of proportion to the signs in the lungs if any (*e*) Early emaciation with the malar flush (*f*) Abdominal symptoms less marked (*g*) Occasional presence of choroidal tubercles (*h*) Presence of other evidences of tuberculosis *e g* pleurisy peritonitis with ascites (*i*) *M tuberculosis* may be occasionally found in the sputum

9 TUBERCULOUS MENINGITIS (*a*) Irregular temperature chart (*b*) Persistence of headache after first week (*c*) Signs of meningeal irritation (*d*) Frequent early vomiting and retraction of the abdomen (*e*) The irritability and curled up attitude in contrast with the apathy and dorsal decubitus of the typhoid patient (*f*) Presence of a clear opalescent or slightly turbid fluid showing cob web formation diminution of chloride (below 550 mg per 100 c c) and of sugar (below 30 mg per 100 c c) increase of protein and lymphocytes and occasionally tubercle bacilli may be demonstrated in cerebrospinal fluid

10 TUBERCULOUS PERITONITIS (*a*) Doughy feel of the abdomen (*b*) Presence of enlarged mesenteric lymph nodes or other tuberculous masses (*c*) Presence of fluid in the peritoneal cavity (*d*) Evidence of coexistent pulmonary lesion

11 ACUTE BACILLARY DYSENTERY (*a*) Sudden onset (*b*) Passage of frequent small stools consisting of mucus blood and pus (*c*) Presence of abdominal pain and tenesmus (*d*) Tenderness over the colon specially the sigmoid (*e*) Characteristic microscopic picture of the stools (*f*) Detection of dysenteric organisms on stool culture

12 SEPTICÆMIC CONDITION (*a*) Sudden onset (*b*) Irregular and fluctuating temperature (*c*) Presence of repeated rigors and sweating with wild delirium (*d*) Rapid feeble pulse (*e*) Leucocytosis (*f*) Presence of some septic foci (*g*) Blood culture positive to organisms other than Bact typhosum

13 INFECTIVE OR MALIGNANT ENDOCARDITIS (*a*) Irregular temperature associated with rigor and marked sweating (*b*) Presence of a valvular lesion though not invariable (*d*) Slight leucocytosis (*e*) Presence of embolic phenomena such as hæmaturia petechiæ and hemiplegia (*f*) Blood culture positive to streptococci or *D pneumoniæ* (*g*) The absence of an organic murmur usually excludes bacterial endocarditis

14 SECONDARY SYPHILIS (*a*) History of exposure to syphilitic infection (*b*) Presence of a penile sore or its scar (*c*) Polymorphic rashes of coppery tint with the characteristic distribution over the trunk and flexor surface of the limbs (*d*) Presence of sore throat with snail track ulcers on the tonsils (*f*) Positive Wassermann reaction

15 LIVER ABSCESS (See page 66)

16 ACUTE APPENDICITIS (*a*) Sudden onset with pain in the epigastrium or round the umbilicus which localises later in the right iliac fossa (*b*) Presence of nausea and vomiting (*c*) Rigidity over the right iliac fossa and tenderness at McBurney's point (*d*) Rapid pulse proportionate to the temperature (*e*) Leucocytosis

17 ACUTE CHOLECYSTITIS (*a*) Sudden onset with rigor and colicky pain over the right hypochondrium (*b*) Rigidity and tenderness over the gall bladder and hepatic areas (*c*) Localised tenderness over the cartilage of the 9th rib often present (*d*) Gall bladder usually palpable (*e*) Presence of Murphy's sign (*f*) Leucocytosis

18 PEL EBSTEIN SYNDROME OR HODGKIN'S DISEASE (See page 66)

19 ACUTE OSTEOMYELITIS (*a*) Tenderness and swelling over the affected bone (*b*) Leucocytosis

20 TYPHUS FEVER (*a*) Sudden onset with rigor (*b*) Soft rapid pulse from the beginning (*c*) Flushed face with injected conjunctivæ (*d*) Early appearance of nervous symptoms such as tremor subsultus tendinum and loss of sphincter control (*e*) Characteristic mulberry rash on 4th 5th day (*f*) Absence of diarrhœa and abdominal tenderness (*g*) Presence of leucocytosis (*h*) Positive Weil Felix reaction

PROGNOSIS

The mortality of typhoid fever varies from 2 to 5 per cent in different epidemics Apart from the virulence of the epidemic the prognosis in an individual case of typhoid fever is influenced by a large number of factors

1 DEGREE OF TOXÆMIA The presence of the following symptoms indicates a severe toxæmia

(*a*) Low muttering delirium with tremors and coma vigil The occurrence of nocturnal delirium only is less serious than the diurnal or the continuous type (*b*) Dry tremulous tongue coated with a thick white brown fur (*c*) Hyperpyrexia (*d*) Unduly feeble and rapid pulse constantly over 130 per minute (*e*) Progressive weakening of the first heart sound Presence of fœtal or gallop rhythm A pulse pressure below 30 mm of Hg (*f*) Marked abdominal distension (*g*) Low urinary output in comparison with the total fluid intake (*h*) Incontinence of urine and fæces

2 PRESENCE OF COMPLICATIONS There are certain complications which indicate an unfavourable prognosis (*a*) Hypostatic pneumonia and bronchopneumonia (*b*) Persistent diarrhœa (*c*) Repeated hæmorrhages from the bowel (*d*) Perforation of the intestine—invariably fatal without immediate operation (*e*) Meningitis—extremely rare (*f*) Suppurative parotitis

3 STATE OF NUTRITION Patients whose nutrition is maintained by an adequate supply of calories protein and fluid do much better than those who are under nourished The latter develop complications more frequently The danger of hæmorrhage and perforation is greater in them

4 GENERAL CONSTITUTION Typhoid fever in obese debilitated and asthenic individuals has a bad outlook Chronic alcoholism is an unfavourable factor in prognosis

5 CO EXISTENCE OF OTHER DISEASES Pre existing diabetes mellitus chronic malaria and kala azar and active pulmonary tuberculosis render the prognosis serious

6 AGE The mortality of typhoid fever is lowest between 5 and 10 years It is high in infants and old people

7 SEX Pregnancy brings about serious complications such as uterine hæmorrhage and septic infections in the course of typhoid fever Abortion or premature delivery occurs at the height of the disease in about 60 per cent of cases

8 WIDAL'S REACTION Delayed appearance or even absence of O agglutinins in the serum of a typhoid patient indicates a bad prognosis (*Felix*)

GENERAL MANAGEMENT

Apart from the specific drug the sheet anchor of treatment consist in a careful nursing of the patient maintaining an adequate nutrition and in anticipating and preventing undesirable symptoms and complications Absolute rest in bed is essential from the beginning of illness till convalescence is well established

The room should be well ventilated and well lighted and it should contain very little furniture The mouth and teeth are to be cleansed before and after each feed with an alkaline mouth wash or some antiseptic lotions *e g* glycothymolin hydrogen peroxide etc and painted with boro glycerin Tepid sponging of the whole body at least once a day is absolutely necessary The pressure points on the skin should be rubbed twice a day with spirit and dusted with talc powder to prevent sores If the skin appears to be reddened over sacrum the patient should be placed over an air ring or better on a water bed When the patient is toxic he should be gently turned on his side every 4 hours to prevent hypostatic congestion of the lungs and the occurrence of bedsores In case of constipation the bowels are to be opened on alternate days by a normal saline enema When there is retention of urine the bladder should be catheterised with strict asepsis The bed pan and the urinal must be used in the recumbent position The stools and urine should be kept for the daily inspection by the medical attendant and their number recorded The temperature pulse and respiration should be recorded 4 hourly

The patient should in no way be allowed to exert himself He should be fed and attended to by a trained tactful and sympathetic nurse

DIET It was a wrong practice to keep the typhoid patient on a starvation diet of lime whey and glucose The resistance of such patients was very low Complications such as delirium intestinal hæmorhage and perforation were frequent Those who recovered were markedly emaciated We know that during fever a patient requires 40 per cent above the basal calories to maintain nitrogen equilibrium and to prevent tissue waste On this basis an adult typhoid patient of average weight should have about 20 calories per pound of his body weight *i e* about 2 500 calories per day In practice however on account of the anorexia toxæmia mental apathy and abdominal disten

sion it is difficult to ensure the intake of a diet of the required calorific value We have often to be satisfied if in the active stage of the disease a diet of about 1 500 calories has been taken Such a diet should consist of a larger amount of easily assimilable non fermentable carbohydrates such as dextrimaltose and a moderate amount of protein in the form of whole milk powdered milk or skimmed milk An adequate supply of vitamins should be ensured For this purpose marmite and orange juice may be given Thus a diet of about 1 500 calories a day may be made up of

Milk	40 oz
Dextrimaltose	4 oz
Orange juice	4 oz
Sugar	2 oz

The feeds should be given in small quantities 6-8 ounces and at intervals of 2 3 hours

In toxic cases with abdominal distension and diarrhœa it may not be possible to give a diet of even 1000 calories a day and we may have to fall back upon lime whey dextrimaltose and glucose for a few days till improvement sets in

In comatose patient adequate nourishment must be maintained by continuous intragastric drip feeding of milk fluids protein etc. If necessary protein hydrolysate may be given by intravenous drip

The diet should be prescribed for each case according to the condition of the bowel For the maintenance of an adequate fluid intake for an adult he should preferably be given about 5 pints in 24 hours An accurate record of the total food and fluid intake and the urinary output in 24 hours should be kept

Mild cases with good appetite and without gastrointestinal complications like vomiting diarrhœa or severe distension may take a more liberal diet during the acute stage Milk puddings custard egg vegetable or meat soup mashed potatoes soft rice bread crumbs boiled or steamed fish may be given according to the appetite and dietary habits of the patient

CONVALESCENCE Typhoid patients should not be hurried through convalescence regarding the diet and getting out of bed During convalescence however it should be the aim to supply a diet of ideal caloric requirements consisting of milk sago puddings bread crumbs biscuits butter lightly boiled eggs custards soups boiled and mashed potatoes boiled fish and fine soft rice The condition of the gastro intestinal tract and the patients likes and dislikes should be carefully

considered before any alteration in the diet and a return to normal diet should be made gradually

The patient should be in bed till the temperature has remained normal for at least ten days The pulse rate and the condition of the first heart sound in the apical area will be useful guides as to when he should sit in a chair Constipation should be treated by enemata which should however be gradually replaced by liquid paraffin to be given orally in doses of one ounce at bed time The administration of general tonics such as strychnine and iron is helpful

SPECIFIC TREATMENT

CHEMOTHERAPY Chloramphenicol originally isolated from cultures of *Streptomyces venezuelæ* has now been synthesized It is a white crystalline substance with bitter taste available in 0 25 g capsule Chloramphenicol has been found to be specific for typhoid fever It was first used in Malaya by Woodward and his colleagues in 1948 in the course of their investigations on scrub typhus

DOSE The previous practice was to use a high dose (about 3 g daily) with an initial loading dose The loading dose has now been omitted and optimum daily dose reduced to 1 to 1 5 g daily in 4 to 6 divided doses for an adult patient This is further reduced to half the amount when the temperature has been normal for 24 hours and continued altogether for 10 14 days Children may be conveniently treated with pædiatric chloramphenicol palmitate containing 125 mg per drachm about 25 mg /kg per day Inspite of alleviation of clinical symptoms bowel lesions take some time to heal and intestinal hæmorrhage and perforation have been known to occur during and after chloramphenicol therapy This explains the need for the usual dietetic and nursing care Relapses are known to be more frequent after chloramphenicol treatment Attempts have been made to reduce it by giving a more prolonged course (as indicated above) In unconscious patients or the children who cannot take the drug by mouth intramuscular injections of chloramphenicol (injectable) may be given in a dose of 0 5 g 12 hourly This is to be replaced by oral therapy as soon as possible

Toxicity Occasional nausea vomiting diarrhœa retention of urine rashes and with heavy dose circulatory collapse may occur Rare toxic manifestations are granulocytopænia aplastic anæmia or purpura The writer has noted 3 cases of confusional psychosis with recovery

The use of Felix s serum vaccine non specific protein and bacteriophage which were in vogue prior to the advent of chloram

phenicol has now been superseded by the latter The injection of small doses of typhoid vaccine however has been suggested for the prevention of relapse after chloramphenicol therapy

SYMPTOMATIC TREATMENT

TOXÆMIA PYREXIA AND HYPERPYREXIA (*a*) *Hydrotherapy* When the temperature rises above 103°F and continues near about that level tepid or cold sponging of the whole body should be carried out 3 or 4 times or more if necessary for 15 20 minutes each time Another useful method of reducing the body temperature with least disturbance to the patient is to cover him with a sheet and then to place over him an ice cradle in which several small buckets of ice or ordinary ice bags are suspended and to cover the whole thing with a blanket The cradle is left in position till the desired effect on the temperature is obtained The traditional use of ice bags on the head is of doubtful value in reducing the temperature Cold packs and cold baths at 65°F have been advocated They are contraindicated in patients with marked prostration cardiovascular weakness severe abdominal pain intestinal hæmorrhage peritonitis and venous thrombosis

Hydrotherapy which is one of the simplest and easily adjustable therapeutic measures when successfully carried out in a rational way appropriate for individual cases has the following effects on the patients

1 Sedative effect on the nervous system *i e* it lessens the delirium tremors etc 2 Increased elimination of toxin through skin and kidneys 3 Tonic effect on the cardiovascular system It improves the cardiac sounds and quality of the pulse and raises the bloodpressure 4 Less chance of passive congestion in the lungs 5 Less chance of bed sores 6 Reduction of temperature 7 Reduction in mortality

(*b*) *Antipyretic drugs* The use of antipyretic drugs such as quinine acid acetyl salicylas phenazone phenacetin and others has now a day been abandoned They are not only useless but in most cases harmful

A simple alkalinising mixture containing potassium or sodium citrate in half or one drachm doses is usually given every 4 or 6 hours to promote heat loss by diaphoresis and diuresis

TYMPANITES In most cases it is a manifestation of intense toxæmia Hence measures against toxæmia will also be effective in relieving the tympanites Application of radiant heat turpentine stupes

over the abdomen turpentine enemata or washing out of the lower bowel by warm normal saline enemata use of a flatus tube and the hypodermic administration of pituitrin or pitres in in doses of ½ ¼ c cm and repeated every four hours for three or four dose are all useful measures and hould be adopted in turn according to the needs of the cases Lastly the diet hould be readjusted and should consist only of calcium whey dextrinalto e and plain water A simple carminative mixture containing oil of cinnamon 2 to 5 minims or spirit cinnamon 15 20 minims is useful

DIARRHŒA It is usually caused by a faulty diet Hence the es ential feature in its treatment is the readjustment of the diet by elimination of milk lactose and fruit juices and their substitution by dextrimaltose calcium whey or lime whey The administration of one dose of 10 grains of Dover s powder or 1 drachm of colloidal kaolin or of bismuth carbonate or both four times a day is useful in checking the diarrhœa

R/

Bismuthi Carbonatis	dr i
Kaolini	dr i
Pulv Tragacanthæ co	gr x
Tr Cardamomi co	m xx
Aquæ Cinnamomi ad	oz i

Sig one dose may be given four times a day

A retention enema containing two ounces of starch solution and half a drachm of tincture of opium may be helpful

Tr Opii	m xxx
Mucilaginis Amyli	oz ii

The loss of fluid due to marked diarrhœa may require intravenous glucose injection or subcutaneous saline injection

CONSTIPATION It is best treated with soap and water enemata or preferably with normal saline enema on alternate days or glycerine and olive oil enema consisting of 2 ounces of glycerine and 4 ounces of olive oil Purgative must never be administered

NERVOUS SYMPTOMS Headache low muttering delirium and restlessness may be relieved by the use of ice caps on the head tepid sponging ice cradling or cold packs which soothes the nervous system Bromides alone or in combination with chloral may be given by the mouth for their sedative action

R/

Potassii Bromidi	gr x
Chloralis Hydras	gr x
Alcoholis	m xx
Syr Aurantii	dr i
Aquae ad	oz i

Sig One dose to be given thrice daily

Calcium gluconate 10 per cent solution 5 c cm may be given intramuscularly for the same purpose For the urgent relief of nervous symptoms sodium luminal gr 3 dissolved in 1 c cm of distilled water should be given subcutaneously and if necessary may be repeated after six hours A lumbar puncture is a valuable method of relieving the meningeal symptoms The intravenous administration of 50 to 100 c cm of 25 to 50 per cent dextrose solution reduces the intracranial pressure and relieves such symptoms

CIRCULATORY FAILURE To prevent circulatory failure it is essential to guard against dehydration of a typhoid patient An adequate fluid intake should be maintained for this purpose In presence of coma and delirium fluid in the form of normal saline with 5 per cent glucose solution should be given by the intravenous drip method or by the subcutaneous route Intravenous plasma or plasma substitutes may be given It must be emphasised however that absorption of the fluid by the rectal route is rather uncertain

In case of circulatory collapse in addition to intravenous fluid therapy stimulants such as pholedrine hyperduric adrenaline neosynephrine or noradrenaline will have to be given

PULMONARY COMPLICATIONS To prevent hypostatic congestion the patient should be turned on either sides from time to time Abdominal distension should be prevented and treated to ensure an efficient action of the diaphragm Bronchitis bronchopneumonia or pneumonia should be treated according to the general principles of treatment by the intranasal administration of oxygen and suitable antibiotics

INTESTINAL HAEMORRHAGE The first essential point in treatment is to ensure absolute physical and mental rest For this purpose the patient is placed in a warm bed with an electric cradle or blanket if required and a hypodermic injection of gr $\frac{1}{4}$ $\frac{1}{2}$ morphine sulphate is valuable Some authorities however do not advocate the use of morphine for fear of masking the signs of perforation if there be

any Local rest of the intestine is also of prime importance because it helps the natural processes of coagulation This object may be achieved by stopping all food by mouth except small pieces of crushed ice or sips of cold water to allay the thirst Feeding by mouth is not resumed till the hæmorrhage has ceased for about 24 hours Application of an ice bag over the right iliac fossa suspended from above may prompt reflex contraction of the intestinal vessel Measures to increase the coagulation of the blood may be adopted Intramuscular injections of 10 per cent calcium gluconate in 5 c cm doses and hæmoplastic sera in 2 c cm doses may be given for this purpose The intravenous administration of 10 c cm of 1 per cent congo red solution has been found to be effective in some cases

To reduce or divert the tendency of hyperæmia from the bleeding area and to maintain an efficient circulation through the brain and heart the foot end of the bed should be raised and in serious cases blood transfusion is essential Where facilities for blood transfusion do not exist the blood loss may be counteracted by the intravenous administration of stored plasma or human serum and in their absence by the administration of plasma substitutes or normal saline with 5 per cent glucose subcutaneously or even intravenously by the drip method Intravenous injection of 10 c c of 30 per cent sodium ascorbate solution may be useful in securing an adequate supply of oxygen to the tissues

As soon as intestinal hæmorrhage is suspected from an abrupt fall of temperature and increased pulse rate the treatment should be instituted immediately without waiting for a hæmorrhagic stool

PERFORATION Immediate laparotomy is the only treatment

PAROTITIS This serious complication is prevented by keeping the mouth scrupulously clean When it occurs hot fomentations or infra red rays may be applied to promote resolution Penicillin is very useful Incision is required if it suppurates

FEMORAL THROMBOSIS Absolute rest to the limb is essential The affected limb should be kept warm by wrapping up in cotton wool and raised on pillows to promote venous return The intravenous administration of 5 10 ounces of sterile 0 5 per cent sodium citrate solution is supposed to relieve pain and to prevent further progress of thrombosis Intramuscular injections of liver extract preparations have been found to be beneficial Anticoagulants like heparin dicoumarol or tromexan may be given but their use may be dangerous unless

properly controlled by a daily estimation of coagulation and prothrombin time respectively

TREATMENT OF RELAPSE

The treatment of relapse is practically the same as that of the original attack

PREVENTIVE MEASURES

The preventive measures against the spread of typhoid fever amongst the individual and in a community consist of the following

1 *Isolation* The patient should be isolated The articles used for his care *e g* feeding utensils thermometer bed pan urinal spittoon douching apparatus sponges towel washing bowls medicine glass etc should all be kept separate

2 *Preventive inoculation of all contacts at the earliest opportunity* It is the most satisfactory and reliable method of checking the spread of an epidemic and conferring individual protection The danger of a negative phase (a phase of lowered resistance to infection) after inoculation during the incubation period has been rather exaggerated In persons incubating the disease the inoculation may be preceded by the administration of Felix anti typhoid serum containing Vi and O antibodies in high concentration

The inoculation is usually made by injecting subcutaneously two doses of a typhoid paratyphoid vaccine prepared from suitable strains of the organisms containing maximum amounts of O and Vi antigen at intervals of 10 days (T A B vaccine)

The first dose contain

Bact typhosum	500 millions
paratyphosum A	250 millions
paratyphosum P	250 millions

in 1 c c and the second dose is injected in double the strength of the first The dose should be proportionate to the age in children Mild local and constitutional reactions *e g* localised pain redness and swelling fever up to 101° 102°F joint pains headache and occasionally vomiting may occur In many there is only transient indisposition The maximum effective response is obtained after about three week of the administration of the first dose of the vaccine The immunity lasts for about 1 2 years but it is desirable that *preventive inoculation should be taken every year*

Besredka s oral method of vaccination is not so effective as the subcutaneous one A bile pill is taken on empty stomach followed

in an hour by the vaccine tablet and this procedure is repeated for three consecutive days Immunity develops within 24 hours of the ingestion of the third vaccine tablet and lasts for about 6 months to 1 year

There is practically no contraindication to inoculation or oral administration of T A P vaccine

3 *Use of boiled water and milk and avoidance of uncooked vegetables or raw fruits during an epidemic*

4 *Disinfection of soiled articles discharges and excreta* The bed clothes and linen should be soaked in 1 in 20 carbolic acid lotion and then boiled for an hour The discharges and excreta should be thoroughly treated by a solution of carbolic acid 1 in 20 for 2 hours or by lysol before final disposal The feeding cups spoon etc should be boiled for 15 minutes

5 *Detection and treatment of carriers* The carriers are diagnosed by carrying out preliminary agglutination tests against H O and Vi antigen of all possible contacts and then examining the faeces urine and discharges and even the marrow fluid for the presence of the enteric group of organisms in those whose blood serum agglutinates the organisms in a titre of 1 10 or higher O agglutination in persons vaccinated more than 2 months ago and Vi agglutination in persons vaccinated with the ordinary T A P vaccine are strongly suggestive of the carrier state Culture of bile obtained by duodenal drainage is one of the best methods of detecting a carrier Negative bacteriological findings however do not rule out the carrier state because the discharge of organisms from the reservoir may be intermittent The carriers should not be allowed to handle food or drink Their treatment by administration of intestinal urinary or biliary antiseptic chloramphenicol autogenous vaccines or even by cholecystectomy is not very satisfactory Some cases respond to a high dose of chloramphenicol—100 mg /kg in 24 hours for seven days None of the recent chemotherapeutic agents or antibiotics has been found to be effective in the successful eradication of the source of infection in a carrier

6 *Care of the contacts* All persons who come in contact with typhoid cases or their soiled clothes or excreta must disinfect their hands by carefully washing them with soap in running water with the help of a nail brush and then with carbolic lotion 1 in 40 or bichloride of mercury 1 in 1 000

PARATYPHOID FEVER

ÆTIOLOGY

Paratyphoid fever is caused by an infection with one of the paratyphoid bacilli Bact paratyphosum A Bact paratyphosum B or Bact paratyphosum C Paratyphoid A infection is more common in India than in Europe where paratyphoid B is prevalent Paratyphoid C type may occur in several varieties The mode of infection the age and sex incidence in paratyphoid fevers are identical with those of typhoid fever The paratyphoid bacilli are however not highly infective and hence a massive dose of infection is necessary for the invasion of the tissue Chronic carriers play a much less important part in its transmission than in case of typhoid fever

PATHOLOGY

The pathological lesions described under typhoid fever also occur in paratyphoid fevers The large intestine is more frequently involved in paratyphoid B infection and catarrhal inflammation without ulceration is rather common There are cases where intestinal lesions may be absent

CLINICAL MANIFESTATIONS

The incubation period mode of onset and the clinical course of paratyphoid fever are almost the same as in typhoid fever except that in the former the course is usually milder and shorter but it is not uncommon to find paratyphoid fever associated with severe toxic *symptoms running a course of six to eight weeks and* clinically indistinguishable from typhoid fever Special clinical features of paratyphoid fever are as follow

ONSET More often sudden unlike that of typhoid fever

SYMPTOMS OF INVASION 1 Nausea vomiting and epigastric pain more common *2 Initial diarrhœa specially seen in paratyphoid B* infection Occasionally the diarrhœa may have all the character of cholera 3 Dysentery 4 Acute catarrh of the upper respiratory tract 5 Shivering and sweating more common 6 Herpes labialis

TOXÆMIA It is usually slight or absent in most cases

TEMPERATURE 1 More variable may be intermittent 2 Maximum height is reached within 3 4 days 3 Defervescence is by rapid lysis in about a fortnight

LIVER May be enlarged and tender

GALL BLADDER May be tender

JAUNDICE May be present

RASH It is said to occur more profusely than in typhoid fever The spot are larger deeper in colour and more irregular in outline

COMPLICATIONS

Cholecystitis catarrhal jaundice pyelonephritis are rather more common than in typhoid fever Pulmonary and cardiovascular complications intestinal hæmorrhage and perforation are rare Pulmonary complications if they occur are more common in paratyphoid A infection than in paratyphoid B Neurological complications such as meningitis encephalitis which are rare in paratyphoid cases may occur not infrequently in paratyphoid B cases Suppurative complications of lungs pleuræ bones joints urinary tract and the subcutaneous tissue are not uncommon Relapses are as frequent as in typhoid fever

PROGNOSIS

As the cour e of paratyphoid infection is usually mild the mortality is much less than in typhoid fever usually about 5 per cent

DIAGNOSIS

Paratyphoid fever may be u pected in presence of one or more of the special features enumerated above But the differentiation from the typhoid fever and the accurate diagnosis of the various types of paratyphoid fevers depend solely on the laboratory finding *e g* blood culture as well as stool culture in the very early stage of the dise e agglutination reaction and urine culture Agglutination titre suggestive of paratyphoid infection in uninoculated persons are

Bact paratyphosum A both O and H above 1 in 50

Bact paratyphosum B O above 1 in 80 and H above 1 in 50

If agglutination in high dilution occurs with only one of the paratyphoid organi ms and there is no agglutination with any other organism the nature of infection is evident In other cases a rising agglutination titre for one particular organism clinches the diagnosis

DIFFERENTIAL DIAGNOSIS TREATMENT AND PREVENTIVE MEASURES

Same as de cribed under typhoid fever

The role of chloramphenicol in paratyphoid fevers has not yet been fully assessed The results of chloramphenicol therapy are not o ati factory as in typhoid fever

J C B

CHAPTER II

DYSENTERY

DEFINITION

Dysentery is a symptom complex characterised by passage of frequent small loose stools containing blood mucus and pus and associated with griping and tenesmus

CLASSIFICATION

1 BACILLARY DYSENTERY Due to (a) *Shigella dysenteriæ* or *Shigella shigæ* (b) *Shigella flexneri* (c) *Shigella sonnei* (d) *Shigella schmitzi*

2 PROTOZOAL DYSENTERY Due to (a) *Entamœba histolytica* (b) Ciliate—*Balantidium coli* (c) Flagellate—*Giardia intestinalis* *Chilomastix mesnili*

3 BILHARZIAL DYSENTERY Due to (a) *S mansoni* (b) *S japonicum* (c) *S hæmatobium*

Bacillary Dysentery

It is an acute infectious epidemic disease caused by specific dysentery bacilli characterised by passage of numerous scanty liquid stools with blood mucus and pus and associated with toxæmia pyrexia griping and tenesmus Some cases may however be mild enough to be regarded as diarrhœa

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is prevalent almost all over the world except in the very cold countries In countries with good sanitation the disease breaks out in small epidemics in school military barracks prisons and mental asylums In the tropical countries the insanitary conditions favour the occurrence of the disease in severe epidemic forms

SEASONAL PREVALENCE Cases of bacillary dysentery begin to crop up in the early summer and in the rainy season reaching the peak of incidence in the autumn

AGE SEX AND RACE INCIDENCE No age is immune But the children are specially liable to be attacked with the disease Dysentery below two years of age is almost always bacillary below ten it is mostly

bacillary and over that age 75 per cent of cases are of bacillary origin Both sexes are equally susceptible The disease has no racial predilection

PREDISPOSING CAUSES Debility lowered vitality fatigue chill errors in diet and drink chronic intestinal disorders and overcrowding under insanitary conditions predispose to the disease

CAUSATIVE ORGANISM Bacillary dysentery is caused by an infection of the bowel with the dysentery bacilli which are non motile non flagellated gram negative organisms akin to the typhoid group There are several types of dysentery bacilli viz

1 *Shigella shigæ* A non mannite fermenter distinct homogeneous group producing both a soluble exotoxin and an endotoxin and giving rise to the severe and fatal forms of dysentery

2 *S flexneri* A mannite fermenter heterogeneous group producing an endotoxin only and consisting of five different serological strains v w x y and z

3 *S sonnei* A late lactose fermenter resembling the Flexner group

4 *S schmitzi* A non mannite fermenter forming indol

The mild types of dysentery or even diarrhoea are caused by *S flexneri* or *S sonnei* Most cases (about 80 per cent) of bacillary dysentery in our country are due to these organisms

Boyd has recently reclassified the organisms in the following way

I Non mannitol fermenting bacilli
  (a) *S shigæ*
  (b) *S schmitzi*

II Mannitol fermenting bacilli
  (a) *S sonnei* a late lactose fermenter
  (b) Two groups of non lactose fermenting organisms—
    (i) Six types of *S flexneri* viz I II III IV V and VI
    (ii) Three types of *S boydi* viz I II and III

Flexner Boyd group of organisms has been found in India the Middle East and New Guinea

MODE OF INFECTION

The dysentery bacilli gain entrance to the large intestine by ingestion of contaminated food or drink Such contamination occurs by one of the following agents

1 HUMAN CARRIERS They are usually convalescent carriers excreting in their stool (3 per cent of cases) more often *S flexneri* than *S shigæ* The dysentery bacilli persist in the muco purulent discharges from the ulcers and also in the retention cysts of the large intestine for a variable period of time usually 4 6 months even 3 years in some cases When such people are engaged as cooks servants or distributors of food and milk they act as important sources of infection and spread the disease

2 FLIES They contaminate food and drink directly by fæcal matter carried in their feet or indirectly by deposition of their own fæces which have been infected with dysentery bacilli as a result of their previous feeding on dysenteric stool

3 WATER SUPPLY Sometimes it is responsible for the spread of the disease It remains infected for 3 weeks when contaminated with the fæces of patients or carriers or by washing of soiled linens

4 Uncooked vegetables and salads may cause infection as human excrement is so often used as manure

PATHOLOGY

On entry into the mucous membrane of the large intestine the dysentery bacilli multiply and liberate a toxin which on absorption and subsequent excretion causes an inflammation of the whole colon the brunt of the attack being specially borne by the sigmoid and rectum In severe cases of dysentery the lower 1 3 ft of the ileum may also be involved The pathological changes vary from mild catarrhal inflammation to a patchy or complete coagulative necrosis of the mucous membrane of the colon In the early stages there are hyperæmia and swelling of the mucous membrane which appears bright red Hæmorrhages may occur in the mucous and submucous tissues The lymphoid tissues are also swollen As a result of intense hyperæmia an outpouring of glairy mucoid and later blood streaked exudate occurs into the lumen of the bowel The crests of folds of the swollen mucous membrane show areas of necrosis covered by greenish fibrinous deposit the separation of which leads to snail track superficial transverse ulcers their edges are ragged but not undermined and the floor is covered with greenish sloughs In some cases with patchy necrosis these ulcers may communicate with one another by submucous sinuses The intervening tissues between the ulcers are red congested and œdematous The whole bowel wall is thickened due to inflammatory œdema and round cell infiltration It is rare for the ulceration to extend deeper into the

submucous tissues and cau e perforation and generalised peritonitis Localised peritonitis may however occur in cases of deep ulceration due to a secondary infection with *Esch coli* or streptococci

There is œdema of the mesentery with enlargement and oftening of the mesenteric glands draining the ulcerated areas

In severe cases the process of necrosis and sloughing is widespread and leads to extensive ulcerated bleeding areas after the sloughs are ca t off In very evere cases gangrene of the gut may re ult The process of repair may start at any stage even before ulceration supervene Healing by resolution and complete regeneration of epithelium occurs in mild cases where ulcers are few and superficial In cases of extensive deep ulcerations healing occurs by granulation and fibrosis which lead to thickening and cicatricial contraction of the bowel and pigmentation

In chronic bacillary dysentery ulcers may be seen in the lower half of the large bowel they are mall lenticular and superficial Occa ionally polypoid masses due to the hyperplasia of the epithelium intervening between the ul ers and retention cysts due to the blocking of the mouths of the Lieberl uhn s follicles by the superficial granula tion tis ue may be present The fluid of the e cysts contains dysentery bacilli in large number In some other cases the mucous membrane of the sigmoid and rectum is often thickened and shows patches of bleeding granulation ti sue In a few cases the large gut completely devoid of its mucous membrane looks like a piece of chamois leather The bowel wall is markedly thickened and partial tenosis is not uncommon Lymphoid peritonitis and exudation of clear serous fluid into the peritoneal cavity may result in some cases

Acute Bacillary Dysentery

CLINICAL MANIFESTATIONS

INCUBATION PERIOD U ually it i 2 to 4 days though it may vary from 1 to 7 days

MODE OF ONSET The onset is usually sudden with varying grade of fever which may be associated with rigor The occurrence of an initial diarrhœa with colicky pains is common Loss of appetite and v miting are often present at the onset Generally the stools become less fæculent more frequent and small in amount contain mucus treaked with blood and become associated with training and tene mus due to the pasm of the internal anal sphincter Soon they con ist entirely of bright red blood mucus and pus

COURSE The subsequent progress depends on the type of the infecting organisms and on the resistance of the individual In cases of *S shigæ* infection the disease runs a severe or fulminating course and is associated with marked constitutional disturbance mainly due to the intense toxæmia and partly due to dehydration

In case of infection by *S flexneri* the course is usually moderately severe or mild In case of infection with Sonne organisms the course is usually mild though it may be acute in some cases specially in children Respiratory symptoms often precede the abdominal symptom in *S sonnei* dysentery

TYPES *Mild Type* (*a*) Toxæmia—slight (*b*) Fever—little or none (*c*) Stool —4 12 in number liquid in character contain slight blood and mucu (*d*) Recovery—in about a week

Moderately Severe Type (*a*) Sudden onset (*b*) Moderately high temperature at first remittent and then intermittent (*c*) Frequent small loose stools 15 30 in number containing bright red blood viscid rose pink mucus and pus with little or no fæcal matter (*d*) Severe colicky abdominal pain tenesmus and dysuria (*e*) Vomiting often present (*f*) Marked toxæmia with signs of dehydration (*i*) Pinched facies with sunken eyes (*ii*) Tongue dry and coated with a brownish white fur (*iii*) Rapid and deep breathing due to an associated acidosis (*iv*) Rapid thready pulse with marked fall of bloodpressure (*v*) Scanty urine (*vi*) Intense thirst and marked prostration (*g*) Tenderness and rigidity over the whole of the abdomen specially over the sigmoid (*h*) Moderate leucocytosis with increase of polymorphs (*i*) Relief of urgent symptoms in 2 3 weeks under efficient treatment

Fulminating Type (*a*) Sudden onset with rigor and vomiting (*b*) High temperature 104° 105°F with a very rapid and thready pulse (*c*) Intense toxæmia with stupor or coma (*d*) Signs of marked dehydration (*e*) Passage of 40 100 stools in 24 hours associated with severe colicky pain and tenesmus The stools have a meat pie appearance due to presence of altered blood and serum Sometimes the stool consist of pure blood and serum only (*f*) Abdomen retracted and tender (*g*) Death occurs in 2 3 days

Gangrenous Type (*a*) Passage of big blackish or gangrenous sloughs in the stools giving out a stinking odour (*b*) Occasional sloughing out of the whole intestine and death from peritonitis

Choleraic Type (*Entero dysentery*) (*a*) Sudden onset with severe vomiting (*b*) Watery and sero sanguineous stools (*c*) Subnormal

temperature (*d*) Early appearance of symptoms of collapse (*e*) Death in 2-3 days

COMPLICATIONS

I EARLY 1 Acute circulatory failure 2 Bronchopneumonia —specially in children 3 Nephrosis 4 Arthritis monoarticular or polyarticular of toxic origin Usually the knee or ankle of one or both sides is affected Effusion in the joints occurs specially in Shiga infection It may be early in the acute stage or more commonly during convalescence The fluid is sterile except in rare cases and agglutinates the dysentery bacilli Recovery almost invariably follows though it may be prolonged 5 Ocular complication — such as acute conjunctivitis iritis and iridocyclitis also of toxic origin occur in the second week 6 Intussusception especially in infants and children 7 Peritonitis and perforation—very rare 8 Parotitis—rare

II LATE 1 Hæmorrhoids 2 Arthritis 3 Ocular complications 4 Pyelonephritis due to *Esch coli* infection 5 Polyneuritis

SEQUELÆ

1 Partial stenosis and dilatation of the large intestine leading to marked constipation 2 Chronic diarrhœa due to irritable colon 3 Vague symptoms of dyspepsia resulting in malnutrition anæmia and emaciation 4 Neuro circulatory asthenia—*i e* palpitation tachycardia disordered action of heart 5 Ascites due to a chronic peritonitis (*Megaw*) 6 Nutritional anæmia and hypovitaminosis due to deficient absorption of nutritional factors

Chronic Bacillary Dysentery

This condition is usually the result of inadequate or inefficient treatment of an acute bacillary dysentery The causative organism of this chronic form of dysentery usually belongs to the Flexner Loyd group

CLINICAL MANIFESTATIONS

TYPES 1 *Mild*—associated with occasional attacks of diarrhœa with mucus or muco pus and symptoms of flatulent dyspepsia

2 *Sever*—characterised by frequent passage of blood stained mucus and necrotic epithelium in stools and presence of marked anæmia emaciation or generalised œdema Abdominal examination in either case often shows tenderness and thickening over the descending colon or sigmoid Symptoms of neurocirculatory asthenia and anxiety

neurosis are commonly present Many of these cases end fatally due to complications such as pneumonia malaria and pulmonary tuberculosis

PROGNOSIS

In acute bacillary dysentery the prognosis depends on the type and virulence of the organism the susceptibility and the constitution of the individual the early diagnosis and efficient treatment Cases of *S shiga* infection if not treated early have a high mortality Cases associated with marked toxæmia continuous high temperature numerous stools (40 50 in 24 hours) containing pure blood and mucus hiccough anuria and signs of marked dehydration have an unfavourable prognosis The mortality is also higher in children and elderly persons than in young adults

In chronic cases of severe type the patients develop progressive anæmia and emaciation and die of asthenia In mild cases patients manifest various symptoms of an anxiety neurosis and require handling with tact and care

DIAGNOSIS

For an early tentative diagnosis of acute bacillary dysentery the clinical data must be carefully considered A naked eye examination of the stools is essential The accurate diagnosis will depend on the following data

ACUTE BACILLARY DYSENTERY *Clinical data* 1 Sudden onset with moderate or high fever accompanied by chill or rigor 2 Presence of moderate or marked toxæmia 3 Nausea or vomiting 4 Colicky abdominal pain 5 Marked tenesmus 6 Rigidity and tenderness over the whole abdomen specially over the descending and sigmoid colon 7 Characteristic stool Frequency—20 to 50 or more Odour—inoffensive or slightly fishy Colour—rose red or like that of meat washings Contents—mucus blood and pus (fæcal matter is absent) Reaction—alkaline

Laboratory data 1 Blood examination—shows a moderate or marked leucocytosis 12 000 20 000 per c mm with increase of polymorphonuclear cells

2 Microscopic examination of the stool—(*a*) Rich cellular exudate showing—

(*i*) 90 per cent of degenerated polymorphonuclear cells

(*ii*) About 4 per cent of non motile macrophage cells with ingested red cells and occasionally leucocytes These are large trans

parent cells derived from the wandering phagocytic cell *They are often mistaken for E histolytica*

(iii) Ghost cells in fair number They are the shadows of polymorphs from which the cell contents have been thrown out

(iv) Red blood cells—either isolated or in normal rouleaux They are unaltered and retain normal size and shape

(v) Intestinal epithelial cells—in large number

(vi) Few bacteriæ

The specimen of stool should be fresh and uncontaminated with urine or antiseptics A bit of blood stained mucus should be chosen for examination and a saline preparation made after proper emulsification

3 Cultural examination of the stool Culture are made in special media from a flake of blood stained mucus obtained from a specimen of fresh uncontaminated stool Positive results are obtained in 70 per cent of cases within the first five days of the onset of the disease A negative report does not exclude bacillary dysentery Recently the use of desoxycholate citrate agar medium has proved to be indispensable in the bacteriological diagnosis of dysentery

4 Serum agglutination The agglutinins develop after 10 12 days of the onset of the disease Hence the agglutination tests are not helpful for an early and rapid diagnosis of acute bacillary dysentery

CHRONIC BACILLARY DYSENTERY *Clinical data* 1 Previous history of an acute dysentery 2 Vague symptoms of dyspepsia 3 Frequent or occasional attacks of diarrhœa associated with griping and tenesmus 4 Presence of mucus and pus in the stools with little or no blood 5 Thickening and tenderness of the descending and sigmoid colon 6 Presence of anæmia and emaciation 7 Absence of response to amœbicidal drugs

Laboratory data 1 Microscopic examination of the stools (*a*) Presence of mucus with scanty pus cells (*b*) Red cells—few or none (*c*) Macrophage cells—either nil or very few (*d*) Bacteriæ—in abundance

2 Cultural examination In chronic cases of dysentery bacilli are isolated from stools with great difficulty in about 26 7 per cent of cases (*Cunningham*) Hence a negative result does not exclude bacillary dysentery Cultures from swabs taken from the ulcers through a sigmoidoscope are likely to yield better results

3 Agglutination tests The agglutination test is of value in differentiating chronic bacillary dysentery from other types of colitis A positive agglutination in titres of at least 1 in 50 against *S shigæ*

1 in 250 against *S flexneri* and 1 in 25 against *S sonnei* indicates a recent or a past infection with the corresponding organisms

4 Sigmoidoscopic examination It is of special value in the diagnosis of chronic bacillary dysentery and in differentiation from chronic amoebic dysentery or from any other form of colitis The scattered patches of bleeding granulation tissue and the narrowing of the bowel associated with rigidity and some pain during the introduction of the sigmoidoscope are the characteristic features of chronic bacillary dysentery

5 Radiological examination The x ray examination of the colon by the barium enema may reveal a loss of haustrations and narrowing or dilatation or sacculation of the lumen of the colon which are in no way distinctive of chronic bacillary dysentery

DIFFERENTIAL DIAGNOSIS

In the *acute stage* bacillary dysentery has to be differentiated from

AMŒBIC DYSENTERY Characterised by

1 Typical clinical findings 2 Characteristic macroscopic and microscopic features of the stool 3 Absence of leucocytosis in an uncomplicated case 4 Sigmoidoscopic findings It is of great value in the differentiation from chronic bacillary dysentery It shows in about 75 per cent cases in the rectum or lower part of the sigmoid characteristic small punched out ulcers with submucous hæmorrhages or scars of healed ulcers the intervening mucosa being healthy An examination of the material from the scraping of the ulcers may reveal *E histolytica*

ALGID TYPE OF MALARIA 1 Very little blood in the stool 2 Icteric tinge of the skin and conjunctivæ 3 Fever and dysenteric symptoms seldom appear simultaneously 4 Spleen often papable 5 Detection of parasites in blood 6 Responds to antimalarial drugs

CHOLERA 1 Usually afrebile axillary temperature often subnormal 2 Stool uniformly watery and of rice water character with small flakes of mucus It may be pinkish being uniformly blood tinged 3 Abdominal pain griping and tenesmus are absent There may be cramps in abdominal muscles Smear and culture show *Vibrio choleræ* in stools

PARATYPHOID FEVER 1 Continued pyrexia 2 Slow pulse in relation to the temperature 3 Presence of the signs and symptom of the enteric group of fevers 4 Blood culture and Widal's test positive to Bact paratyphosum A or B

ACUTE BACTERIAL FOOD POISONING 1 History of a simultaneous affection of many of the persons within a short period of partaking the same food 2 Constant presence of vomiting in the early stage 3 Presence of blood in stools is uncommon 4 Occurrence of a rash either erythematous or urticarial or rarely purpuric 5 Presence of organisms of the Salmonella group on culture of stools and vomitus 6 Positive agglutination reaction against *Salmonella enteritidis* or *Salmonella aertrycke* or other organisms in 4-5 days

URÆMIC COLITIS 1 Usually afebrile 2 Characteristic clinical picture of uræmia 3 Characteristic urinary findings 4 Increase of non protein nitrogen and urea in blood

HENOCH S PURPURA 1 Presence of purpuric spots in the limbs 2 Presence of urticaria and pain in the joints which may be swollen 3 Thrombocytopenia may be present

INTUSSUSCEPTION 1 Usually in infants and young children 2 Sudden onset 3 Usually afebrile at least at the onset 4 Palpable mass over ascending colon 5 Absolute constipation for the first few days followed by passage of bright red blood and mucus in the stools 6 Other signs of obstruction

BALANTIDIAL DYSENTERY 1 Very rare 2 Emaciation—very marked 3 Detection of *Balantidium coli* or its cysts in the stool

In the *chronic stage* the differential diagnosis has to be made from the following

CHRONIC AMŒBIASIS (See under Amœbiasis)

TUBERCULOUS ENTERITIS 1 History of prolonged illness with progressive emaciation usually febrile 2 Stools loose and profuse containing mucus and pus and even blood 3 Evidences of tuberculosis elsewhere 4 Detection of *M tuberculosis* in stool

HEAVY HELMINTHIC INFESTATIONS 1 Presence of characteristic ova in large number in stools 2 Eosinophilia 3 Anæmia

SPRUE 1 Pale bulky frothy motions 3 to 5 in number especially in the morning 2 Red glazed tongue 3 Emaciation 4 Anæmia usually of a macrocytic and hyperchromic type

FLAGELLATE DYSENTERY (GIARDIASIS) 1 Frequent occurrence of a lienteric diarrhœa 2 Presence of abdominal discomfort and flatulence 3 Presence of large pale stools and undigested residue 4 Detection of *Giardia intestinalis* in stools

INTERNAL HÆMORRHOIDS 1 Dull aching pain during and after

defæcation 2 Passage of bright red blood after defæcation 3 Digital and proctoscopic examination are diagnostic

RECTAL POLYPUS 1 Occasional occurrence of profuse hæmorrhage with bright red blood and mucus in stools 2 Griping and tenesmus uncommon 3 General condition of the patient good 4 Digital or sigmoidoscopic examination will reveal the growth

MALIGNANT DISEASE OF THE PELVIC COLON AND RECTUM 1 Incidence in elderly people 2 Emaciation anæmia and constipation 3 Signs of dissemination elsewhere 4 Proctoscopic or sigmoidoscopic examination will perhaps reveal a fungating growth 5 Presence of a filling defect in the colon with narrowing of the lumen by an x ray examination with barium enema

Rectum should always be examined in every case of dysentery specially in elderly persons

DIVERTICULITIS 1 Common occurrence in obese and elderly persons 2 Presence of a tender swelling in the left iliac fossa associated with muscular rigidity and frequency of micturition 3 Presence of barium filled diverticula on x ray examination after the evacuation of a barium enema

TREATMENT

The main principles of treatment of acute bacillary dysentery are (*a*) to conserve the energy of the patient by rest (*b*) to neutralise or reduce toxæmia (*c*) to ensure rest to the bowels by elimination of irritating toxic material and by administration of a suitable non irritating liquid diet (*d*) to combat dehydration and (*e*) to secure symptomatic relief

GENERAL MANAGEMENT

REST Absolute bed rest is essential to maintain the strength and energy of the patient The patient should use bed pan and urinal in the recumbent position In severe cases with very frequent stool the bed pan even should not be used A pad of cotton wool or tow is put under the buttocks and gently changed whenever soiled and burnt to prevent the spread of infection The duration of rest varies with the severity of the case Even for a mild case rest in bed should be maintained for about a fortnight as the ulcers take 10 12 days to heal In chronic cases also rest in bed is necessary Care of the mouth and toilet of the skin are essential

WARMTH In cold weather a flannel binder over the abdomen or

a hot water bag will give much comfort to the patients In chronic cases cold baths should particularly be avoided

Previously saline purgative in repeated doses was the standard treatment In addition to a mechanical flushing out the saline mixture reduced the congestion and oedema of the intestine and relieved the pain and tenesmus After the introduction of specific sulpha drugs the use of saline purgative which tends to exhaust the patient who is already dehydrated has practically been abandoned

In chronic cases constipation should be avoided the bowels should be kept regularly open by the use of half to one ounce of liquid paraffin at night *Ishapgulha* seeds in doses of 2 3 heaped table spoons are useful laxatives Abdominal massage along the course of the colon will help to maintain the intestinal tone and promote normal peristalsis

DIET In acute cases the patient should have only boiled and cooled water in adequate quantities for 12 hours Then glucose or dextrimaltose should be added to the water in 10 per cent strength With improvement thin arrowroot or barley water rice gruel and sago puddings may also be given Feeds should be given in quantities of 4 6 ounces every 2 3 hours Gradually skimmed milk and lactic acid milk with 10 per cent dextrimaltose are allowed In older children with the disappearance of the toxic symptoms some authorities advocate the use of grated pulp of raw apples in daily quantities of 12 25 ounces for a few days before the addition of lactic acid 1 immed milk or skimmed milk Recently apple powder in 4 to 8 per cent suspension in boiled water without the addition of any sugar is being used The beneficial results of the apple diet have been attributed to (*a*) the toxin absorbing action of pectin protopectin and cellulose (*b*) the sedative and astringent effects of the organic acids and (*c*) the m chanical cleansing action of the bulky cellulose During convalescence solid food is given when the patient has been free from symptoms for about 7 days Regarding diet patient should never be rushed through convalescence as indiscretion in diet may lead to relapse

In cases of chronic bacillary dysentery a bland and non irritating low residue diet of high caloric value is important and it should consist of a large amount of protein moderate amount of carbohydrate and only a small amount of fat In addition it should be rich in vitamins For this purpose boiled fi h chicken soft boiled eggs liver soup milk soft boiled rice mashed potatoes may be allowed Coarse vegetables and raw fruits are to be avoided Orange juice bananas grated pulp of apple baked *bæl* are useful additions

It is essential that the patient should strictly adhere to this diet for about six months otherwise relapses may occur

SPECIFIC TREATMENT

CHEMOTHERAPY *Sulphaguanidine* The treatment of bacillary dysentery has been revolutionised by the introduction of sulphanilyl guanidine also known as *sulphaguanidine* It is a sulphonamide compound which is moderately soluble in water and yet poorly absorbed from the gut so that if orally administered it is excreted in the stool in high concentrations and can exert its bacteriostatic activity on the dysenteric organisms

Dose Initial dose of 0 1 g per kilogram body weight followed by a maintenance dose of 0 05 g per kilogram of body weight every 4 hours at first and every 6 hours as the number of stools is reduced

Mode of Administration In an average Indian adult 8 10 tablets (0 5 g each) are to be given orally initially and 4-6 tablets every 4 hours for about 1 2 days or till the number of stools is markedly reduced. Thereafter 4 tablets should be continued every 6 hours until the stool have been normal in number and consistency for 2 days The duration of treatment should not exceed 12 days but if necessary the course can be repeated after a week. The tablets should be crushed before administration

A prolonged courses of sulphaguanidine for 2 weeks or more should be given and repeated as required in chronic bacillary dysentery The broad spectrum antibiotics or oral streptomycin may also be used Medicated enema specially sulphaguanidine retention enema is very helpful

Succinylsulphathiazole and *Phthalylsulphathiazole* are even more poorly absorbed than sulphaguanidine and are very effective in the treatment of bacillary dysentery and should be the drugs of choice The recommended average dose is 20 g daily for succinylsulphathiazole and 12 g daily for phthalylsulphathiazole for not more than 7 days Succinylsulphathiazole is more effective than sulphaguanidine in the treatment of Sonne dysentery and in the eradication of carriers harbouring *S sonne*

Sulphadiazine or *sulphadimidine* in a dosage of 4 to 8 grammes daily is very useful These drugs have the advantage that a smaller dosage than that of sulphaguanidine or succinylsulphathiazole is effective The disadvantage is that these drugs cannot be used with impunity in dehydrated patients until the fluid balance has been restored

End results If administered within the first three days of the illness the results are uniformly good the fever comes down to normal in 2 days toxæmia disappears the stools become free from blood and mucus and the diarrhœa ceases in 2 3 days Lyon reports good results in 75 per cent cases of dysentery in children If treatment is begun after the third day results are less satisfactory The drug is not *so useful in chronic bacillary dysentery*

Streptomycin is effective in the treatment of bacillary dysentery After oral administration it is not absorbed but exerts its local effect on the bacteria in the intestine The newer antibiotics aureomycin terramycin and chloromycetin are also active against the dysentery bacilli These antibiotics however do not appear to be in any way superior to the sulpha drugs

BACTERIOPHAGE THERAPY Its value in the treatment of bacillary dysentery is very doubtful and it has been abandoned since the introduction of chemotherapy

SEROTHERAPY The scope for antidysenteric serum has become limited since the introduction of sulphaguanidine in the treatment of bacillary dysentery Serotherapy perhaps is indicated in some severe cases of shiga infection Refined and peptonised concentrated antishiga serum should be given in such cases in a dose of 100 000 to 200 000 international units or more daily for 2 3 days Intravenous administration with ½ 1 pint of 5 per cent glucose in normal saline is preferable to intramuscular or subcutaneous routes In children the serum may be injected intraperitoneally in ½ pint of normal saline

It should be emphasised that serotherapy if indicated is not a substitute for but should supplement chemotherapy with sulphaguanidine

LOCAL TREATMENT

RECTAL IRRIGATION In chronic cases of bacillary dysentery rectal irrigation with suitable bactericidal and comparatively non irritating fluids is an essential method of treatment to wash out the intestine of toxic material and to promote healing of the ulcers in the rectum and the sigmoid colon It gives much relief and comfort to the patients by reducing tenesmus and the frequency of stool Half to one ounce of castor oil is given at bed time A preliminary cleansing enema of two pints of warm sodium bicarbonate solution (60 grains to a pint) is given in the following morning An hour later the foot end of the bed is raised and the medicated enema of 16 ounces is run very slowly at a temperature of 100 110°F into the rectum through a soft rubber

catheter (No 12) attached to a graduated cylindrical glass funnel held at a height of 1 2 feet above the pelvis The patient should be lying on the left side and he may change to the right side later He should be encouraged to retain the enema as long as possible Silver salts should not be retained for more than half an hour The enema should be repeated on alternate days for a fortnight It may then be followed by a retention enema of warm olive oil 10 oz and bismuth subgallate ½ oz for ten consecutive nights

CHOICE OF DRUGS Various drugs have been recommended for bowel lavage The following are some of the useful ones

Sulphaguanidine Sulphaguanidine (1 g per oz) suspended in 6-10 oz of water and mucilage may be given daily as retention enema.

Silver Salts These are preferred in cases of ulceration. Silver nitrate is used in gradually increasing strengths from 1 to 5 grains per ounce of distilled water Rogers recommends albargin (silver albuminate) in the strength of 1 grain to an ounce of cold distilled water Unlike silver nitrate it is painless and yet quite effective

Chiniofon (1 2 per cent solution) It is especially indicated when the dysentery bacilli are obtained on culture of the stools or material taken from the ulcers through a sigmoidoscope

Eusol (5 oz to 1 pint of saline) *and Permanganate* (1 gr to 1 pint) They are indicated in presence of secondary infections

Normal Saline and Sodium Bicarbonate Solution (2½ per cent.) These are simple non irritating solutions which shall be used when the ulcers have healed and only the scarring and congestion persist.

Cæcostomy (the operation of choice) appendicostomy or ileo tomy may be done and colonic lavage may be carried out in the same way to promote healing of the ulcers by ensuring rest to the large bowel and by direct antiseptic action of these drugs used for lavage The cæcostomy wound is closed a few months after sigmoidoscopic examination has shown healing of the ulcer and the patient has been free from pain and has shown marked clinical improvement.

SYMPTOMATIC TREATMENT

GRIPING 1 Hot water bags or turpentine stupes over the abdomen

2 Injection of sodium luminal gr 3 and atropine sulphate gr 1/100 hypodermically in severe cases

3 R/

Potassii bromidi	gr xv
Tinct belladonnæ	m v
Tinct hyoscyami	m xv
Spt chloroformi	m xx
Aquæ cinnamomi ad	oz 1

Sig one dose t d s

TENESMUS 1 Starch and opium enema 2 Morphine suppositories 3 Gentle rectal lavage with warm normal saline 4 Hypodermic injection of morphine hydrochloride gr $\frac{1}{6}$ only in severe cases associated with sleeplessness and exhaustion

VOMITING AND HICCOUGH 1 No feed except sips of plain water by mouth 2 Maintenance of adequate fluid intake by subcutaneous injection of normal or hypotonic saline with 5 per cent glucose 3 Atropine sulphate injection or chlorpromazine 10 mg t d s orally 4 Mustard plaster over the epigastrium

RESTLESSNESS AND SLEEPLESSNESS 1 Oral administration of a mixture containing potassium bromide and chloral hydrate in doses of gr 15 each

2 Hypodermic injection of sodium luminal gr 3 dissolved in 1 c cm of distilled water

3 Morphine hydrochloride g $\frac{1}{8}$-$\frac{1}{4}$ hypodermically may be given when the patient is worn out for want of rest and sleep due to severe abdominal pain griping and tenesmus

COLLAPSE AND DEHYDRATION 1 Application of warmth to the limbs

2 Intravenous administration of 1-2 pints of normal or hypertonic saline necessary in severe and urgent cases of the choleraic type This may have to be repeated Transfusion of blood plasma or plasma substitutes has proved to be of great value in such cases

3 Subcutaneous administration by the drip method of one to two pints of normal saline with 5 per cent glucose in less severe cases

4 Intramuscular injection of 1 c cm of veritol or diffusible stimulants *e g* 2 c cm (500 mg) of caffeine and sodium benzoate solution

TREATMENT OF COMPLICATIONS

ANÆMIA It is an important complication of chronic bacillary dysentery and unless it is properly treated healing of the ulcers is delayed Anæmia may be successfully treated by

1 Oral administration of ferrous sulphate 12 to 18 grains a day or ferri et ammonii citras gr 90 a day

2 Intramuscular injection of 2 c cm of crude injectable liver preparations daily if the anæmia happens to be macrocytic

3 Oral administration of dr 1 of marmite with orange or tomato juice three times a day

4 Blood transfusion in severe cases with hæmoglobin below 40 per cent

ARTHRITIS 1 Immobilisation of the affected joint by splinting 2 Application of Scott s ointment 3 Hot fomentation 4 Gentle massage 5 Aspiration only in cases of marked effusion

IRIDOCYCLITIS 1 Application of ½ per cent atropine sulphate lotion as eye drops 2 Use of eye shades

PREVENTIVE MEASURES

The following measures should be adopted for the prevention of the spread of bacillary dysentery

1 Early detection of cases of acute bacillary dysentery and their isolation 2 Careful washing and disinfection of hands of all contacts 3 Disinfection of soiled linen clothes and other articles used in care of the patient 4 Disinfection of stools before their disposal 5 Use of boiled water and milk 6 Protection of food and drink against contamination by flies 7 Detection of carriers by stool examination and agglutination tests their isolation and treatment 8 Improved sanitation and proper disposal of sewage In rural areas the use of bored hole latrine is strongly recommended

P B B

CHAPTER III

CHOLERA

[Cholera asiatica]

DEFINITION

It is an acute infectious disease usually epidemic though sometimes endemic in certain areas caused by *V cholerae* (*Vibrio comma*) and characterised by profuse purging of rice water stool vomiting marked dehydration muscular cramps collapse and suppression of urine

CLASSIFICATION

Vibrios

- Group A
  Cholera and cholera like vibrios common H antigen but divided into sub-groups by specific O antigens the important one being sub group I
  - True cholera vibrios
    Non hæmolytic
    - Inaba
    - Ogawa
- Group B
  Other vibrios biochemically and serologically distinct less fermentative action
  - Hæmolytic (cholera like)
    El Tor vibrio

Ogawa and Inaba types are common whereas another type Hikojima is very rare

The status of hæmolytic El Tor vibrio has been the subject of much discussion Observations of de Moor (1938) on the Celebes outbreak of 1937 indicated that El Tor vibrio was probably the causative organism of cholera there But in India El Tor vibrio is not the cause of cholera

The vibrios can grow in milk and survive in water as long as three weeks It is killed quickly by drying and exposure to sun light though on moist linen it may survive for a week

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION Cholera is endemic in lower West Bengal East Pakistan and Assam especially in towns or inland ports on big rivers There are other endemic areas in India such as the

eastern part of Bihar the Uttar Pradesh the Madhya Pradesh the south east areas of Madras and the Konkan Coast of Bombay Outside India cholera is endemic in certain areas of the Federated Malaya States the Dutch East Indies Vietnam Thailand and the Philippines

In Europe the disease occurred as minor epidemics in the Balkans in 1913 and also during the World War I Europe was first visited by cholera in 1830 the spread occurred by the land route from India to *South Russia via Afghanistan and Persia Since then about* five epidemics had spread to Europe from India either by the land or by the sea

SEASONAL PREVALENCE In Calcutta and other parts of West Bengal the disease usually reaches its peak of incidence in end of April In the Punjab the maximum incidence occurs in May Rise of absolute humidity about 0 400 and diminished rainfall in the previous monsoon or in winter associated with inadequate water supply favour the outbreaks of cholera in the endemic areas and a study of these two factors may enable one to correctly forecast the occurrence of epidemics a few months beforehand

AGE SEX AND RACE INCIDENCE Young adults are the usual victims though the children and the aged do not escape

Males are more frequently affected than females The people of all races are equally susceptible to the disease

PREDISPOSING CAUSES 1 Living in overcrowded areas under highly insanitary conditions as in slums and pilgrim centres

2 Chronic intestinal disorders

3 Lowering of the gastric acidity by fasting

4 Ingestion of irritating food or drink or over ripe fruits

5 Taking of saline purgatives

6 *Exposure to chills*

CAUSATIVE ORGANISM Cholera is caused by an infection with *V cholerœ* discovered by Koch in Egypt in 1883 and confirmed by him in 1884 in the Medical College Calcutta It is a gram negative motile organism with one terminal flagellum curved like a *comma* 1 5 to *2 microns* in length and 0 5 *micron* in breadth The organisms may show s shaped or spirillar forms according as two or more than two are united end to end They grow in all ordinary media but especially luxuriously in 1 per cent alkaline peptone water within *6 to 8 hours*

with the formation of a surface pellicle *V cholerae* can be recognised by its characteristic comma shape on staining with dilute carbol fuchsin (1 in 10) and its property to produce indol and nitrites in alkaline peptone water and to give rise to a positive cholera red reaction by the formation of nitrosoindol on the addition of pure sulphuric acid Besides it is nonhæmolytic and agglutinable in as high a titre as 1 in 10 000 by a specific group I O anti cholera serum prepared by intra venous injections of living or killed group I O vibrios into rabbits True cholera vibrio ferments mannose and sucrose but not arabinose In this connection it may be emphasised that *V cholerae* has two types of antigens—(*a*) heat labile flaggellar H and (*b*) heat stable somatic O O antigen is the characteristic component of true cholera vibrios Almost all severe epidemics of cholera are due to the O strains of *V cholerae* The cholera vibrio also gives rise to Pfeiffer s reaction characterised by bacteriolysis in the peritoneal cavity of an immunised rabbit In some cholera patients towards the end of the epidemic certain vibrios (paracholera vibrios) have been isolated and found to be hæmolytic and not agglutinable by the specific anti cholera serum

MODE OF INFECTION

V cholerae gains entrance to the intestinal tract in one of the following ways

INFECTED WATER SUPPLY It is the commonest cause of explosive epidemics of cholera which is mainly a water borne disease The authenticity of this view has been amply corroborated by the severe outbreak of cholera in Hamburg in 1892 through the pollution of its unfiltered water supply from the river Elbe and the very low incidence of the disease at Altona though situated down the same river because of its filtered water supply Epidemics in India usually occur due to contamination of the water supply from river unprotected tanks and wells by the washing of soiled clothes and utensils and throwing of excreta

CHOLERA CARRIERS There are two types of cholera carriers —

(*a*) *Contact carriers* The contact or apparently healthy carriers have usually no symptoms except mild diarrhœa in some cases and they constitute about 2 per cent of the healthy persons who come in contact with cholera patients

(*b*) *Convalescent carriers* About one third of the convalescent carriers may discharge virulent comma vibrios in the stools during the first week of their convalescence and thus be potent sources of dissemi

nating the disease far and wide along the routes of human intercourse and along trade routes with the help of the speedy methods of communication of modern times The disease may break out amongst the pilgrims when they gather together in the holy places under insanitary conditions The convalescent persons or even the contacts are responsible for spreading the disease among the people of various places they pass through on their homeward journey

The carriers spread the disease usually by contamination of food and drink during the preparation or handling of food They may also infect the water supply of rivers tanks and wells by the washing of their soiled clothes and throwing of their excreta

FLIES They play an important role in the transmission of the disease by directly contaminating food and drink Occurrence of sporadic cases and also of protracted epidemics is common in insanitary parts of a town and in places with bad conservancy arrangements favouring the breeding of flies

CONTACT INFECTION Sometimes a direct infection may take place from contact with the patients or the infected articles

PATHOLOGY

Under conditions which reduce the acidity of the gastric juice the cholera vibrios pass through the stomach to the lower part of the small intestine where they multiply in the alkaline medium liberate an endotoxin which is absorbed into the circulation and produces the characteristic symptoms and signs of cholera The production of a *soluble exo-toxin has been reported by some workers* but it has not been definitely confirmed by others

INTESTINE The toxins act locally on the mucous membrane of the small intestine causing an intense hyperæmia of the mucous surface and swelling and enlargement of the solitary lymphoid follicles and the Peyer s patches There is also catarrhal inflammation followed by desquamation of the epithelial cells and exudation of a serous fluid with small flakes of mucus suspended in it thus giving rise to the typical rice water stools In some severe cases exudation of a sero sanguineous or even purely sanguineous fluid may occur The submucosa is not usually penetrated by the vibrios except in fatal cases Ulceration perforation and invasion of the blood stream practically never occur The peritoneal surface is markedly congested and the mesenteric lymph nodes are frequently swollen and enlarged due to proliferation of the mononuclear cells The mucous membrane

of the stomach and duodenum may show congestion and petechial hæmorrhages

GALL BLADDER AND LIVER The inflammation may spread up the duodenum and bile ducts to the gall bladder which may show characteristic changes of acute cholecystitis in about 4 per cent of cases The infection in the gall bladder may persist for 2 4 weeks after convalescence and an intermittent discharge of vibrios may occur in the bile and thus in the stools of carriers The toxins on absorption may so damage the liver cells that the secretion of bile is inhibited The bile in the gall bladder becomes viscid and thick due to severe lo s of fluid The vomit and the stools of the cholera patients are colourless and watery Absence of colour is probably due to excessive dilution

LUNGS They are dry due to dehydration the blood in the pulmonary vessels is thick and tarry Small and scattered pneumonic patches may occasionally be found Pulmonary œdema and localised areas of emphysema are common

KIDNEYS The kidneys how hyperæmia of the medulla and swelling of the cortex The tubular epithelium shows cloudy swelling hyaline and fatty degeneration The lumen of the tubules may be occluded by a coagulated material The changes in the kidneys are indicative of a toxic nephrosis and not of acute diffuse nephritis We are of definite opinion that the failure of renal function in cholera is due to the severe dehydration associated with the loss of fluid and chloride by frequent and copious purging and vomiting with consequent decreased filtration pressure Besides in a follow up study of many convalescent patients of cholera we have seen no evidence of nephritis on examination of the urine Recently pallor of the cortex with congestion of medulla and juxtamedullary glomeruli have been observed by special stains (De) This suggests that the renal disorder in cholera is of the same nature as in other renal anoxia syndromes Bilateral cortical necrosis has also been observed

BLOOD CHANGES Due to the marked loss of fluid and salts the following changes occur in the blood

1 Reduction of blood volume and consequent rise of the specific gravity from the normal figure of 1056 to as much as 1072

2 Increased white cell count (15 50 000 per c mm) with increased percentage of polymorphs diminution of lymphocytes and increase of large monocytes

3 Increased red cell count (6-8 000 000 per c mm) with rise of hæmoglobin percentage due to hæmo concentration

4 Rise of the non protein nitrogenous bodies such as urea uric acid and creatinine in the blood due to deficient renal excretion as a result of dehydration

5 Rise of phosphate ions in blood for the same reason and consequent diminution of the alkali reserve The alkali reserve is further reduced by the loss of bases in the stools

6 Sodium and chloride concentration of plasma are normal Potassium is elevated in the stage of suppression of urine

MORBID ANATOMY

The following are the characteristic findings on autopsy of patients who have died of cholera

1 Presence of early *rigor mortis* 2 Dryness of all serous sacs 3 Rose red colour of the peritoneum due to marked congestion of the intestinal mucous membrane especially of the ileum with swollen lymphoid follicles 4 Presence of rice water stools or occasionally of uniformly blood tinged stools in the lumen of the intestine 5 Enlarged mesenteric lymph nodes which often show necrosis 6 Distended gall bladder containing thick and viscid bile 7 Presence of dark thick blood in the veins and the right heart Petechial hæmorrhages in the pericardium 8 Dry and shrunken lungs occasionally showing areas of congestion and œdema 9 Congested kidneys 10 Empty urinary bladder 11 Muscles appear dark and firm 12 Enlargement of thymus—almost a constant finding (*MacCallum*)

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually 1 2 days though it may vary from a few hours to 5 days

MODE OF ONSET The onset is usually sudden sometimes it is preceded by prodromata such as diarrhœa vomiting lassitude and mental depression

The clinical features in a typical case of cholera may be described in three stages *viz* (1) the stage of evacuation (2) the stage of collapse and (3) the stage of reaction

STAGE OF EVACUATION In this stage the patient who is usually a young healthy adult begins to pass frequent and loose motions which are at first fæcal but quickly lose their fæculent character and become

colourless watery and copious Small flakes of mucus soon appear in the watery motions and give rise to the typical rice water appearance The stools if allowed to stand in a conical glass show clear watery fluid at the top and flocculent granular material at the bottom Sometimes the stools may be sero sanguineous The passage of stools is profuse and painless and rarely associated with griping and tenesmus Vomiting which at first consists of undigested food and bile but soon becomes watery and copious is an important feature The patient is prostrated out of proportion to the number of stool Cramps in the calf muscles may appear in this stage

STAGE OF COLLAPSE OR ALGID STAGE As a result of marked loss of fluid by profuse vomiting and purging this stage is characterised by signs and symptoms of dehydration superadded to those of toxæmia such as

1 The cyanotic pinched facies with sunken eyes and cheeks

2 Restlessness associated with intense thirst a burning sensation of the body and severe painful cramps in the muscles of the limbs abdomen and even of the whole body These cramps are mainly due to the loss of chlorides and water from the muscle tissues

3 Vomiting and purging may continue even in this stage

4 Coldness and clamminess of the skin of the whole body The surface temperature is subnormal though the rectal temperature may vary from 99°F 101 F The fingers and toes are livid and shrivelled like those of a washer woman The voice is husky and feeble

5 Rapid and shallow respirations with a rapid and thready pulse which is later imperceptible The systolic blood pressure falls as low as 70 to 65 mm of Hg In majority the blood pressure can not be recorded The specific gravity of blood rises as high as 1072

6 Suppression of urine followed by signs and symptoms of uræmia such as dirty heavily coated tongue with a foul smell irritability of temper mental apathy slow and deep respiration or periodic respiration mental confusion and muttering delirium followed by muscular twitchings and occasionally convulsions

The algid stage may last for a few hours or for 2 3 days Then it may terminate in death from uræmia or it may be followed by the stage of reaction or sometimes by a speedy convalescence

STAGE OF REACTION In favourable cases the stage is characterised by the following features

1 Diminution in the number of stools with the appearance of

bile in them 2 Cessation of vomiting 3 Improvement in the general appearance with fulness of the face 4 Return of urinary *secretion which is at first scanty and contains albumin and casts* 5 Return of pulse at the wrist with improvement in the cardiac sounds and the blood pressure 6 Rise of skin temperature to normal or above normal occasionally preceded by a chilly sensation or rigor

In unfavourable cases there is hyperpyrexia or the temperature may rise upto 102°F and may assume a remittent character as in typhoid fever and gradually the patient may pass into a state of coma (*cholera typhoid*) This is due to marked absorption of toxins from the small intestine as a result of the improved circulation

In other cases due to a prolonged collapse stage the renal circulation is impaired and hence the patient develops symptoms of uræmia

CLINICAL TYPES

There may be wide variations from the above typical clinical picture according to the virulence of the organism the resistance of the individual and the severity of the epidemic The following are the main clinical types

1 MALIGNANT OR ASIATIC CHOLERA (*Cholera gravis*) It is usually seen at the peak of epidemics Its clinical features have been described above

2 CHOLERAIC DIARRHŒA (*Cholerine*) It is usually characterised *by the absence of algid symptoms and of suppression of urine*

3 DRY CHOLERA (*Cholera sicca*) This type is frequently seen in old and debilitated persons The patient usually dies of rapid collapse without any actual purging or vomiting At autopsy the bowels are seen to be distended with a large amount of rice water material Death in these cases is due to an embolism or thrombosis of the pulmonary vessels caused by sudden and excessive viscosity of the blood consequent on the profuse exudation of serum into the lumen of the bowels

4 AMBULATORY TYPE (*Cholera ambulans*) In this type which is found in all epidemics apparently healthy persons with few or no symptoms *discharge cholera vibrios in their stools Such persons are* responsible for the spread of the disease

5 CHOLERA TYPHOID This type is occasionally seen during the stage of reaction in severe cases of Asiatic cholera Its clinical features have already been described

COMPLICATIONS

1 Acute circulatory and cardiac failure especially during early convalescence 2 Uræmia 3 Pulmonary œdema—commonly seen in the elderly people due to left ventricular failure In other cases it may result from the increased permeability of the pulmonary capillaries due to the action of the cholera toxin 4 Bronchitis and broncho pneumonia 5 Enteritis and paralytic ileus 6 Hiccough 7 Hyper pyrexia—rare

SEQUELÆ

1 Anæmia and asthenia 2 Chronic entero colitis 3 Suppurative parotitis 4 Corneal ulcers 5 Gangrene of different parts of the body formerly common but now rare under modern methods of treatment 6 Bed sores 7 Miscarriage or abortion in pregnant women—almost invariable 8 Cholecystitis—not common Jaundice—occasionally

PROGNOSIS

The mortality varies widely from 12 16 per cent in adults and 20 to 50 per cent in children in different epidemics and also in the earlier and later stages of the same epidemic

The prognosis in an individual case is based on a consideration of the following factors

1 *Age*—Children and old persons do badly

2 *Constitution*—Patients who are ill nourished and asthenic succumb easily to the disease

3 *Pre existing diseases*—Diseases of the kidney heart and liver render the prognosis grave

4 *Pregnancy*—The mortality is increased in pregnant women due to the danger of abortion or premature delivery and the associated septic complications

5 Presence of one or more of the following complications is associated with a bad prognosis

(*a*) Rapid recurrent or prolonged collapse

(*b*) Complete suppression of urine

(*c*) Symptoms of uræmia

(*d*) Hyperpyrexia and a rectal temperature above 102°F in the collapse stage

(*f*) Marked tympanites

(*g*) Blood pressure below 100 mm of Hg in the reaction stage

6 *Response to treatment*—Prompt and efficient treatment adopted in the early stages will considerably reduce the chance of death in an individual case

7 *Whether previously inoculated with specific cholera vaccine*—The mortality rate in the inoculated is reported to be lower than that of the uninoculated

DIAGNOSIS

During an epidemic it is not difficult to make a diagnosis of cholera Sporadic and atypical cases of cholera may be definitely diagnosed on a consideration of the following

CLINICAL DATA 1 Profuse painless evacuations of rice water material

2 Profuse vomiting of colourless watery fluid without nausea or retching

3 Presence of marked dehydration and collapse associated with the characteristic facies

4 Prostration out of proportion to the number of stools

5 Appearance of muscular cramps

LABORATORY DATA 1 *Microscopic examination* of a sample of fresh stool shows

(*a*) Mucus and abundant degenerated epithelial cells with few leucocytes and macrophages

(*b*) Actively motile comma shaped organism showing the fish in stream appearance in a hanging drop preparation or comma shaped or s shaped vibrios on staining with dilute carbol fuchsin (1 in 10) for about a minute

2 *Cultural examination* Alkaline peptone water is inoculated with a flake of mucus from the stools and incubated for 8 12 hours The surface growth is examined for the vibrios the nature of which is confirmed by the typical morphology non hæmolysis and agglutination in a titre of 1 in 1000 by a standardised specific group I O anti cholera serum

3 *Blood examination* (*a*) Presence of a high leucocytosis

(*b*) High specific gravity due to marked concentration of the blood

(*c*) Agglutination test—It is of very little value in the early diagnosis of cholera because O agglutinins appear in the serum of cholera patients 8 12 days after the onset of disease

DIFFERENTIAL DIAGNOSIS

Atypical and sporadic cases of Asiatic cholera have to be differentiated from the following diseases

1 ACUTE GASTRO ENTERITIS (*a*) Presence of abdominal pain and griping (*b*) Presence of nausea and retching with vomiting which contains bile (*c*) Presence of bile in the stools (*d*) Absence of marked prostration and collapse and dehydration (*e*) Absence of suppression of urine

2 ALGID MALARIA (*a*) History of previous attacks of fever (*b*) Pallor and anæmia (*c*) Icteric tinge in the conjunctivæ (*d*) Presence of an enlarged spleen and liver though not constant (*e*) Presence of bile in the vomit and stools which are usually not so profuse as in cholera Besides vomiting precedes diarrhœa (*f*) Presence of malaria parasites in the blood (*g*) Response to anti malarial therapy

3 CHOLERAIC TYPE OF ACUTE BACILLARY DYSENTERY (See under Dysentery)

4 SIMPLE OR SPORADIC CHOLERA It is usually mild and feebly infectious

5 CHOLERA MORBUS (*Cholera nostras*) It is an acute gastro-enteritis with vomiting diarrhœa and muscular cramps occurring in the summer and autumn due to errors in diet

6 ACUTE BACTERIAL FOOD POISONING (*a*) History of taking tinned or contaminated food (*b*) Simultaneous affection of all or some of those who had shared the same food (*c*) Presence of nausea retching and vomiting which precede the diarrhœa (*d*) Slight or moderate fever with headache (*e*) Presence of abdominal pain griping and tenesmus (*f*) Presence of mucus and blood in the stools The stools are never watery and colourless (*g*) Urticarial or sometimes purpuric rashes on the skin

7 PNEUMONIA WITH DIARRHŒAL ONSET (*a*) Onset with pain in the chest and a high temperature (103° 104°F) (*b*) Rapid shallow respirations with inspiratory dilatation of the *alæ nasi* (*c*) Characteristic lung signs (*d*) Presence of bile in the stools

8 ACUTE ARSENICAL POISONING (*a*) Presence of burning pain over the epigastric region associated with nausea and vomiting which contains food particle bile mucus and streaks of blood (*b*) Colicky abdominal pain Diarrhœa following vomiting (*c*) Presence of

mucus and occasionally streaks of blood in the stools (*d*) Muscular cramps not usual (*e*) Detection of arsenic by medico-legal tests in vomit urine and stools

9 CORROSIVE SUBLIMATE POISONING (*a*) Burning pain in the mouth and throat with presence of white patches due to corrosion of the mucous membrane (*b*) Vomiting precedes diarrhœa and often contains blood and mucus (*c*) Stools contain blood and sloughs of necrotic mucous membrane (*d*) Detection of mercury by chemical tests in the vomit and stools (*e*) Appearance of stomatitis gingivitis adenitis and salivation if the patient survives the acute stage

10 MUSHROOM POISONING (*a*) History of taking mushroom (*b*) Presence of fragments of mushroom in the stools (*c*) Urticaria

11 TRICHINOSIS (*In acute stage*) (*a*) Presence of colicky pain (*b*) High eosinophilia (*c*) Presence of *Trichinella spiralis* in stools

GENERAL MANAGEMENT

REST AND WARMTH Rest in bed is essential till convalescence is well established The warmth of the body should be maintained by the use of blankets and hot water bottles over the extremities

DIET All food should be withheld for about 24 hours except small sips of boiled and cooled water *dab* (green cocoanut) water or pieces of cracked ice to allay thirst With cessation of vomiting and watery diarrhœa barley water with 5 per cent glucose is given Gradually calcium whey and skimmed milk are added The return to normal diet should be cautious and gradual

SPECIFIC TREATMENT

There is no specific therapy available which has any definite advantage over treatment with fluid and salts only

CHEMOTHERAPY Sulphaguanidine is often used in the treatment of cholera and several workers have reported better results when it is combined with intravenous saline treatment Its value however is doubtful Bhatnagar *et al* reported satisfactory results with formosulphathiazole a condensation product of sulphathiazole and formaldehyde but this has not been confirmed by others Lahiri found that mortality could not be reduced by supplementing the usual therapeutic measures with sulphaguanidine formosulphathiazole or formosulphacetamide and these drugs had no vibriocidal action *in vivo* Chloromycetin (oral or intravenous) caused rapid disappearance of *V cholerae* from the stools

but did not influence the ultimate recovery rate (Chaudhuri *et al*) The action of terramycin (oral) was similar (Da *et al*)

Sero therapy vaccine therapy bacterio phage therapy and intestinal antiseptics have been used previously from time to time but their value could never be clearly demonstrated They have now been abandoned

In view of absence of effective specific remedies the essential aims in the treatment of cholera are (1) to prevent and combat dehydration (deficiency of water and chlorides) and concomitant collapse (2) to restore the alkali reserve to normal (3) to relieve distressing symptoms as they arise and (4) to treat complications

SYMPTOMATIC TREATMENT

TREATMENT OF DEHYDRATION AND COLLAPSE AND MAINTENANCE OF FLUID AND ELECTROLYTIC BALANCE Whenever a cholera patient comes under observation we should assess the degree of dehydration by a general examination and by an estimation of the blood pressure the specific gravity of the blood and the red cell count

The specific gravity of the blood may be estimated with the help of a series of small bottles containing solutions of glycerine and water of different specific gravities increasing by 2 per bottle from 1056 to 1070 or by copper sulphate solution of varying specific gravity The blood from the pricked finger of a cholera patient is sucked into a capillary pipette and a drop of blood is very gently squeezed into the centre of the fluid in the specific gravity bottle If the drop sinks to the bottom the specific gravity is higher and if it floats up to the surface the specific gravity is lower than that of the fluid in the bottle When the blood has the same specific gravity as the fluid in the bottle it neither sinks nor floats up

A systolic blood pressure reading below 80 mm of Hg blood specific gravity over 1060 or presence of circulatory collapse associated with restlessness a feeble thready or imperceptible pulse at the wrist cyanosis and cramps indicate dehydration

It is evident that the primary object of treatment in cholera is to replace the fluids and electrolytes lost through the stools and vomits and to maintain biochemical equilibrium till the patient gets over the crisis In case of acidosis alkaline saline will have to be given Administration of fluid should however be strictly controlled in cases of persistent suppression of urine and uræmia after the patient has recovered from the stage of shock and collapse (See uræmia) Rogers's hypertonic saline is still the routine treatment for cholera

The *hypertonic saline* consists of 120 grains of sodium chloride and 4 grains of calcium chloride in a pint of distilled water The method of administration is as follows The hypertonic saline should be administered at the room temperature 80°F This precaution will minimise the risk of rigor and hyperpyrexia following saline transfusion The amount of the saline solution will depend on the specific gravity of the blood 1 pint for a specific gravity of 1061 2 pints for 1062 3 pints for 1063 More than 3 pints at one sitting are not administered even though the specific gravity is above 1063 because of *the danger of cardiac embarrassment In children more* than 10 ounces should not be given at one time If necessary the saline injection is repeated by drip till the establishment of renal secretion and return of the pulse at the wrist A rise of the blood specific gravity to 1063 or over and a recurrence of copious evacuations are also indications for a repetition of the saline injections On the average a moderately severe case of cholera requires 4 injections of hypertonic saline in 24 hours In case of prolonged collapse which is associated with a diminished alkali reserve of the blood in about 80 per cent of cases one pint of alkaline normal saline *i e*

Sodii bicarbonatis	gr 160
Sodii chloridi	gr 90
Aquæ destillatæ	pint 1

should be first given slowly by intravenous route and then the hypertonic saline solution should be run in to make up the total quantity of fluid as indicated by the specific gravity

Sometimes 100 c cm of 25 per cent glucose solution in sterilised ampoules may be added to one pint of alkaline saline with advantage

The *preparation of alkaline normal saline* requires great care The solution should not be boiled for fear of converting the sodium bicarbonate into sodium carbonate which is toxic Sodium bicarbonate should be wrapped in paper and then sterilised in an autoclave before dissolving in sterile normal saline or water In places where facilities of sterilisation do not exist the salt may be baked in a clean dish before preparing the solution To obviate the practical difficulty of sterilising sodium bicarbonate 140 c c of 7½ per cent sodium bicarbonate solution available in sterilised ampoules may be used in place of 160 grains of sodium bicarbonate for preparing one pint of alkaline saline

The *route of choice* of saline administration is always intravenous At first attempt should be made to give intravenous saline by closed method failing which open method should be adopted

The *rate of flow* of the saline solution into the vein should be four ounces per minute for the first pint and two ounces per minute for next two pints to avoid the occurrence of rigors Appearance of cardiac distress headache and cough indicates the necessity of further slowing the rate of flow

For subsequent transfusions normal saline containing 5 per cent glucose (prepared by adding the contents of six 25 per cent 25 c c glucose ampoules to one pint of normal saline) should be used Hyper tonic saline and alkaline saline should be repeated only when the patient continues to have excessive vomiting and purging with reappearance of signs of severe dehydration and collapse Under such circumstances the patient should first receive 15 ounces of hypertonic saline and then 30 ounces of alkaline saline

Indications for stopping or slowing the saline transfusion

1 Pyrogenic reaction A careful watch should be kept on the rectal temperature Any tendency to a rise should be immediately over come Indeed no intravenous transfusion should be given if the rectal temperature is 101°F or above until the temperature is lowered by iced sponging cold bowel wash etc 2 Præcordial pain or distress 3 Headache and 4 Dyspnœa or cough

In some cases intravenous transfusion may be continued at a slower rate after the above signs and symptoms have disappeared But in others where the signs and symptoms persist saline should be continued if required by the subcutaneous route

CIRCULATORY COLLAPSE 1 Measures to combat dehydration are essential Percorten (*d soxycorticosterone acetat*) in 10 20 mg dosage may be given by the intramuscular route Human plasma 250 500 c cm has also been advocated for averting an impending vasomotor failure

2 Circulatory stimulants like pholedrine or noradrenaline may be injected when required

Alcohol should not be used because of the peripheral vasodilatation caused by it

MUSCULAR CRAMPS 1 Replacement of lost fluid and salts by the hypertonic saline transfusion is the most effective remedy 2 Massage and warmth 3 A small hypodermic injection of morphine hydrochloride or inhalation of small doses of chloroform has been advocated by some authorities when the cramps are very severe

The belief that morphine predisposes to uræmia is not borne out by recent work

PERSISTENT VOMITING 1 Hypodermic injection of atropine sulphate gr 1/100 is very useful 2 Pieces of cracked ice to suck 3 In intractable cases largactil 25 to 50 mg may be given Avomin 1 tablet at two hourly interval may also be tried

TYMPANITES Normal saline bowel wash passage of flatus tube and intramuscular injection of prostigmin 1/60 1/24 gr or 0 25 1 mg often give relief If a flatus tube is not available ordinary rubber catheter may be used

URÆMIA If the anuria persists and the patient develops signs of uræmia *e g* drowsiness dyspnœa often with a hissing type of respiration after the dehydration and collapse have been corrected by suitable saline transfusion no further saline should be given The patient should then receive only two pints of 10 per cent glucose solution in 24 hours given intravenously by drip method This solution can be easily prepared by adding 250 c cm of 25 per cent glucose solution from sterilised ampoules to 350 c cm of distilled water Saline should not be given to these cases Fruit juices are best withheld at the stage of anuria Diuretics should not be used Penicillin may be given for lung complications

In cases of persistent suppression of urine with uræmia after the patient has recovered from shock and collapse amount of fluid administered should be carefully balanced and Bull s regimen of treatment for renal anoxia syndrome appears to be the most suitable (See page 102)

TREATMENT OF COMPLICATIONS

HYPERPYREXIA 1 Repeated cold sponging of the whole body 2 Ice cradling 3 Iced saline enema 4 Withholding of intravenous saline transfusion till temperature is lowered by the measures

RIGOR 1 Avoidance of transfusion of saline at a temperature higher than 80°F when rectal temperature is above 100°F 2 Avoidance of transfusion at a rapid rate 3 Use of freshly prepared pyrogen free *distilled* water in preparing the *saline solutions*

HICCOUGH 1 Correction of dehydration acidosis and uræmia 2 Intravenous administration of glucose 3 Administration of atropine sulphate gr 1/100 hypodermically 4 Largactil—25 50 mg 5 Application of mustard plaster over the epigastrium

6 ℞

Hydrargyri subchloridi	gr ¼
Sodii bicarbonatis	gr ii
Mentholis	gr ¼
Chloretoni	gr ii

Fiat pulvis

Sig One powder to be taken every half an hour for 2 hours

PULMONARY ŒDEMA 1 This is usually due to excessive fluid and sodium chloride administration This should be withheld 2 Temporarily oxygen inhalation is helpful

Bronchopneumonia parotitis corneal ulcers and other complications should be treated by appropriate measures

PREVENTIVE MEASURES

At the modest computation the total number of deaths annually in India during a cholera epidemic amounts to about four hundred thousands This is a serious economic loss to the country specially in view of the fact that cholera takes its toll on the healthy adults at the prime of their lives Cholera is a preventable disease and hence it is the duty of every medical man to prevent it effectively

The method of controlling the disease consists of personal and general prophylaxis

PERSONAL PROPHYLAXIS 1 *Anti cholera inoculation* The method is of great value in protecting the individual and the community The vaccine should be made from the local strains of *V choleræ* which are smooth virulent and contain specific immunising heat stable O antigen and are killed by heat at 55°C Each cubic centimetre contains 8000 millions killed organisms with 0 5 per cent phenol The initial dose is ½ c cm given by the subcutaneous route followed a week later by the second dose of 1 c cm In mass prophylaxis a single dose of 5 8 000 millions of bacilli will confer protection for 6 months and reduce the incidence of disease by 50-75 per cent In India vaccines containing Inaba and Ogawa strains have definitely reduced the cholera incidence The injections cause mild local and systemic reactions The Japanese workers have recommended the use of sensitised vaccines for prophylaxis because (*a*) large doses may be given with little or no reaction and (*b*) the production of immunity is more rapid

2 Maintenance of an efficient general health by avoiding chills fatigue over work dietetic excesses and prolonged starvation

3 Use of boiled milk and boiled water for drinking purposes

4 Avoidance of uncooked vegetables and raw fruits

5 Protection of all food and drink against contamination by flies

6 Disinfection of hands of contacts *e g* medical attendants nurses and relatives

7 Disinfection of all excreta soiled clothes and articles used in the care of the patient

General Prophylaxis These measures should be carried on by the public health department

1 Early notification

2 Strict isolation of the cholera patients

3 Sterilisation of drinking water of tanks and wells by

(*a*) Reservation (*b*) Treatment with bleaching powder or potassium permanganate

4 Adequate supply of potable drinking water where sterilisation is not efficient or not possible

A M

CHAPTER IV

LEPROSY

[Elephantiasis græcorum]

DEFINITION

Leprosy is a chronic infectious disease caused by the *Mycobacterium lepræ* and characterised by diffuse or nodular infiltrations of the skin mucous membranes and nerves resulting in local anæsthesias muscular atrophies contractures deformities and trophic ulcers

HISTORY

The disease has been prevalent in India China and Africa for several thousand years It existed as early as 3000 B C in Egypt as is found from the study of the Ebers papyrus In ancient India it can be traced as far back as 600 B C during the time of Sushruta The Græco Roman period (50 B C) had leprosy according to Themison of Laodicea who was the first to describe leprosy known as *elephantiasis græcorum* at that time A clear description of the disease was given by Aretæus in 1st century A D The existence of the disease can be traced in China and Japan from 7th and 8th centuries A D respectively

The modern clinical account by Boeck appeared as late as 1847 and in 1871 Hansen discovered the bacillus causing leprosy

The disease apparently originated in Egypt then spread to Arabia and the Middle East countries India China Japan and Far Eastern regions Crusaders were responsible for the spread of the disease throughout Europe and England and the post Columbian period saw the spread of the disease to America

In the middle ages leprosy was rampant in different parts of Europe but the adoption of stringent measures for the segregation and isolation of lepers was very successful in preventing the spread of the disease which since then gradually declined in Europe

ÆTIOLOGY

Geographical Distribution At present leprosy seems to be a disease particularly of tropical and sub tropical countries The disease is very widely distributed in India China and South Africa It is very difficult to make a correct estimate of the number of lepers because the early or latent cases often escape recognition and moreover many lepers wilfully hide the loathsome disease According to recent

census there are about 10 12 million lepers all over the world of which the largest number is found in Africa. The incidence varies from 0 5 2 5 per cent in West Bengal. It is very high where the soil is dry and laterite (Bankura Birbhum Midnapore Purulia).

AGE AND SEX INCIDENCE. Recent investigations by intradermal lepromin test and by careful studies into the family history of lepers show that children under ten years are very susceptible to infection because of the low natural immunity and also because of the close contact with the infectious leprous parents and relatives. Thus infection occurs almost exclusively in infancy and childhood. Adult infection is very rare. The disease however manifests itself usually between 10 12 years of age reaching its peak of incidence at 30 and showing a gradual decline afterwards. It rarely occurs after 40 although no age is entirely exempted. Both sexes are equally liable till the age of 15 years. After the 25th year the males show a preponderance possibly due to their greater chance of exposure to infection and of coming under observation.

OCCUPATION. It has no definite influence over the incidence of the disease unless it affords opportunities of coming in close and prolonged contact with infectious type of leprosy.

PREDISPOSING FACTORS. 1 *Prolonged and intimate contact with an infective case* is a major factor in the spread of the disease. Opportunity for such a close contact may occur by living with a leper in the same house or in the same room by attending on a leper by having a sexual relationship with a leper lying in the same bed with leprous parents husband or wife or by mixing with lepers. The disease though propagated by contagion is however not highly contagious.

2 *Lowering of the natural resistance*. As already mentioned the resistance is low in childhood. Debilitating diseases dietetic deficiencies and overcrowding under poor hygienic surroundings and low economic status all tend to lower the resistance and render a contact susceptible to the disease.

3 *Heredity*. At one time it was supposed to play an important role in the causation of leprosy. The tendency of the disease to run in certain families gave rise to the belief that it was a hereditary disease. The theory of hereditary transmission is untenable.

CAUSATIVE ORGANISM. The disease is caused by *Mycobacterium lepræ* discovered by Hansen in 1871. It is a non motile rod shaped

acid fast bacillus 0 5 to 0 2 *micron* in breadth and 1 8 *microns* in length having the same morphological features and staining reactions as the *Mycobacterium tuberculosis* from which it differs as follows

1 Lepra bacilli are very easily found in stained smears often in enormous numbers and in clusters 2 They are more frequenly observed intracellularly 3 They are deeply stained but less acid fast 4 They have not yet been successfully cultivated *in vitro* 5 Leprosy has not been successfully transmitted to animals by inoculation

MODE OF INFECTION

CONTAGION 1 Prolonged and intimate contact with infective cases is not essential though risk of infection is greatest Repeated intimate contact is also sufficient Susceptible individuals may develop the disease from infrequent occasional or short or even a single contact It has been estimated that only 3 per cent of people living with lepers show clinical evidences of the disease 2 Cutaneous abrasions or wounds caused by insect bites or other minute lesions may serve as portals of entry for the bacilli which are present in the nasal discharges and in discharges from the leprous sore of infectious patients

2 Infection may occur in 2 4 per cent of cases through sexual intercourse as a result of close bodily contact

Accidental inoculation is very rare It may be due to

A *Direct contact*

B *Indirect contact*—Infection through contaminated fomites

PATHOLOGY

On gaining entrance into the body probably through a minute cutaneous abrasion the micro organisms spread along the fine fibres of the cutaneous nerves to the plexuses in the skin There after depending on individual immunity and resistance the lesion may completely heal or may progress to invade either the skin or the peripheral nerves The lepra bacilli then invade the lymphatics of the corium and sub cutaneous tissues whence they may be carried to the neighbouring lymph nodes and then even to the blood stream under conditions which markedly lower the general resistance Many of the bacilli are destroyed by the phagocytes during their transport others multiply under favourable conditions and give rise to the characteristic granulomatous lesions known as *lepromata* A leproma consists of large vacuolated mono nucleated or multi nucleated giant cells containing enormous masses of lepra bacilli usually called the lepra cells surrounded by large mono

nuclear epithelioid cell plasma cells and fibroblasts Caseation and necrosis are absent due to the low toxicity of the lepra bacilli and to the better blood supply of the granuloma These granulomatous infiltrations are usually seen near the hair follicles sweat gland and the blood vessels of the skin and they give rise to the characteristic painless subcutaneous nodules and glabrous anhydrotic patches The cut surface of these nodules has a smooth glistening greyish white appearance

MUCOUS MEMBRANES The mucous membranes of the upper respiratory tract septum of the nose conjunctivæ mouth tongue pharynx and larynx are prone to heavy invasion in lepromatous leprosy resulting in thickening and ulceration

PERIPHERAL NERVES The bacilli at first invade the sensory nerve endings in the skin producing anæsthetic patches and gradually ascend along the sensory cutaneous branches to the nerve trunks where they grow and multiply in the peri and endo neurium producing granulomatous infiltrations and leading to marked irregular thickening The axis cylinder and later the myelin sheaths show evidences of degeneration The posterior root ganglia the anterior horn cells the sympathetic ganglia the gasserian ganglia may all be involved and show degenerative changes

BONES The bones specially the small bones of the hands and feet show atrophic changes due to damage and destruction of the sympathetic nerve fibres or by pressure of the granulomatous tissue

LYMPHATIC GLANDS They are involved *via* the lymphatics of the skin or the nerves and show varying degrees of enlargement due to chronic inflammatory changes The juice obtained on puncture of the superficial lymph nodes may show lepra bacilli

EYES They may be involved The eye lesions comprise infiltrations of the eyelids corneal ulceration and subsequently opacity iritis and iridocyclitis leading ultimately to loss of sight

LIVER AND SPLEEN The liver and rarely the spleen are affected and enlarged especially in nodular leprosy Fatty and amyloid changes occur

LUNGS Upper respiratory passages are involved This may extend down the bronchi and bronchioles

KIDNEYS A toxic or amyloid nephrosis is not uncommon in the advanced cases of nodular leprosy

TESTES AND OVARIES In most of the advanced cases of leprosy the testes and less frequently the ovaries show fibrosis due to leprotic changes The infection has peculiar selectivity for the male gonads

HISTOLOGICAL TYPES During recent years careful histological study of various lesions of leprosy has shown a few characteristic patterns In the skin the changes are found in the dermis the changes in the epidermis being only secondary to the pressure effects of underlying granuloma in the dermis The following type are usually seen

1 *Tuberculoid Type* This pattern is characterised by granuloma formation consisting of foci of epithelioid cells surrounded by small round cells with one or more giant cells of Langhans type in the centre Acid fast bacilli are very scanty This granuloma may infiltrate the subepidermal zone of the dermis There is both perineural and endoneural infiltration The epithelioid cells usually do not show any marked degree of vacuolation Involvement of peripheral nerves and ganglions is very early in this type

2 *Lepromatous Type* This type is characterised by loose granuloma consisting of small round cells and epithelioid cells with marked vacuolation resulting in the formation of characteristic foamy or lepra cells The subepidermal zone of the dermis is practically free from infiltration and there is usually no endoneural infiltration

3 *Dimorphous (Intermediate Borderline) Type* Here the histological pattern does not conform to one single type All kinds of combinations of the above two types may be seen

CLASSIFICATION

Leprosy has been classified clinically for a long time into lepromatous and neural types Based on individual resistance and reaction (Leprosy Congress Rio de Janeiro 1946) leprosy is now classified into three broad types

I Lepromatous—(*a*) Macular (*b*) Infiltrated (*c*) Neuritic

II Tuberculoid—(*a*) Macular (*b*) Infiltrated (*c*) Neuritic

III Dimorphous—(*a*) Macular (*b*) Infiltrated (*c*) Neuritic

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is rather long and varies from 2 to 5 years the average being 3 years The more intimate the contact and the more susceptible the individual the shorter is the incubation period

MODE OF ONSET It is usually insidious because of the vague and

transient initial manifestations and because of the painless character of the primary skin lesion

I LEPROMATOUS TYPE *Prodromal stage* It may be indefinite but in others it is characterised by

(i) repeated attacks of irregular fever with rigor and excessive sweating

(ii) chronic dry rhinitis with occasional epistaxis

(iii) recurrent attacks of dyspepsia and diarrhœa

(iv) progressive weakness

(a) *Macular lesions (Stage of primary eruption)* After a variable period of the prodromal stage a macular eruption which constitutes the first manifestation of the disease (*the primary lesion*) appears on the body In most cases the lesions are multiple small raised circular erythematous patches scattered all over the body with a symmetrical distribution The edge of the lesion is not well defined but merges with the skin The palms of the hands and the soles of the feet are very rarely affected These smooth erythematous patches may disappear leaving a brown discolouration or subsequently they may become hyperpigmented hypopigmented or depigmented and hairless

This stage of the primary eruption is followed by a variable quiescent phase Under conditions of lowered resistance the disease progresses actively due to multiplication of the lepra bacilli and passes into the next stage

(b) *Infiltrated lesions* This stage may or may not be preceded by a definite macular stage The essential clinical features of this stage are firstly recurrent attacks of fever with fresh eruptions or with extension of the previous skin lesions secondly thickening of the skin in patches often at the sites of old macules due to spread of the infiltration to the deeper layers of the skin and thirdly the formation of nodules (*lepromata*) which vary in size from a pea to a bean are discrete or coalescent The nodules appear on face sides of the nose lobes of ears back of hands and feet trunk extensor surfaces of arms groins and genitals In most cases of leprosy in men the breasts are hypertrophied The nodules feel soft and smooth and are devoid of hairs They vary in colour and in size according to the phases of the disease During the quiescent phase they may have the natural colour of the skin in the reactionary phase they look red swollen and inflamed and new crops of nodules appear with the production of toxæmia and fever During the subsequent phase of resolution they look dark

brown in colour and may undergo absorption leaving circular scars In advanced cases the coalescence of the nodules on the face and the associated extensive thickening of the skin give rise to the repulsive leonine appearance The ultimate fate of the nodules varies according to the resistance of the individual and the degree of the infection If the infection is heavy due to rapid multiplication of the lepra bacilli and the resistance low the nodules may break down ulcerate and even suppurate

The mucous membrane of the septum of the nose is involved sooner or later It may be swollen inflamed and ulcerated and there may be difficulty in breathing through the nose The ulceration may extend deeper causing a necrosis of the septal cartilage and thus depression at the bridge of the nose An offensive blood stained or mucoid discharge may occur from the nostrils and it is a very common source of infection The nasal swab is always bacterio logically positive At one time the nasal mucous membrane was regarded as the site of the primary lesion but recent work emphasises that it is not affected before the skin

The ulcerative process in the nose may spread down the nasopharynx to the buccal cavity and larynx

The eyes and the various internal organs such as testes liver spleen lungs and kidneys may also be involved in this type of leprosy

With the increase of body resistance however the bacilli tend to invade the nerve trunks the skin lesions may subside the nerve lesions may appear the nasal and skin lesions gradually cease to discharge lepra bacilli and thus the patient gradually becomes non infective

II Tuberculoid Type *Prodromal stage* It is often well marked though it may be short or absent Usually the patient complains of the following (i) Lassitude (ii) neuralgic pains (iii) sensory dis turbances like hyperæsthesia paræsthesia and anæsthesia over the face inner sides of the hand and forearms and outer aspects of the legs and feet

(a) *Macular lesion* (*Stage of primary eruption*) It is charac terised by the appearance of single large macular eruption which consists of hypopigmented patches situated usually over the back buttocks extensor surfaces of the limbs and the face The distribution is asymmetrical The centre of the patch is dry the edge is a well defined pigmented hyperæsthetic ring encircling a pale and usually anæsthetic area The well defined edge clearly demarcates healthy from

non healthy skin The affected areas are also characterised by loss of hair and absence of sweating

Usually there is no absolute loss of sensation in these patches from the very beginning *The order in which the superficial sensations are generally impaired is first light touch then heat and lastly pain sensations* When the anæsthesia extends deeper into the tissues and is complete the patient feels nothing even if the affected parts are incised with a knife The anæsthetic patches are due to the involvement of the cutaneous nerves by the leprotic infiltration which ascends along the small terminal sensory nerve fibres

(*b*) *Infiltrated lesion* Gradually the infection reaches the nerve trunks by ascending along the nerve fibres or from the blood stream and spread by the perineural lymphatics producing irregular nodular thickening in course of the affected nerves The nerves that are commonly affected are the ulnar peroneal and great auricular less commonly the median radial brachial the seventh and the fifth cranial nerves and the cervical nerves

These nerves when passing over a bone and lying very superficial can be felt as thickened cords which are at first tender and hyperesthetic The patient may complain of acute neuralgic pains associated with a sense of numbness in the parts supplied by the affected nerves and accompanied by moderate or high fever *The lymphatic glands of the affected area may be swollen*

This is a benign and stable stage The nodules are erythematous and elevated above the skin surface The sensory loss is asymmetrical

(*c*) *Neuritic lesions* (*Stage of contractures and trophic changes*) With the progress of the disease anæsthesia nerve enlargement weakness and atrophy of muscles contractures and trophic changes appear

If the ulnar nerve be affected it is felt as a thickened cord at the bend of the elbow and it produces loss of sensations on the ulnar side of the hand and forearm muscular wasting of the hypothenar eminence the interosseous spaces and the half of the forearm and a claw hand with marked contracture of the ring and little fingers When the peroneal nerve is affected it may be felt as a thickened cord as it winds round the fibula Loss of sensation is present over the lower two-thirds of the outer aspect of the leg and the dorsum of the foot upto the base of the toes which are slightly flexed Foot drop associated with inversion is the characteristic feature

In the affected area all the muscles are not equally involved and

so curious distortions may be met with Involvement of the 7th nerve causes facial paralysis ptosis of the upper lid and eversion of the lower lid due to muscular atrophy Thus the eye cannot be closed Ulceration of the cornea results from constant exposure and corneal anæsthesia due to 5th nerve involvement Opacity and loss of sight follow

Trophic ulcers may appear in the fingers some or all of which may drop off X rays may show thinning or necrosis of the phalanges Perforating ulcers of the feet and destruction of the bones of the toes may be present in cases where the nerves in the lower extremity are involved

III DIMORPHOUS TYPE This variety is quite common The disease may begin as a lepromatous type and gradually the nerves are involved *in the later stages producing trophic lesions Commonly skin* and nerve lesions may appear simultaneously Rarely the neural type may be followed by lepromatous manifestations

The essential features of lepromatous tuberculoid and dimorphous leprosy are shown in tabular form on page 285

COMPLICATIONS

LEPROMATOUS TYPE 1 Laryngeal involvement leading to laryngeal stenosis 2 Visceral involvement especially the leprotic involvement of the testes leading to sterility in most advanced cases 3 Corneal ulceration and iridocyclitis 4 Leprotic reaction 5 Pneumonia 6 Pulmonary tuberculosis—a very common cause of death in leprosy 7 Nephrosis (amyloid)

TUBERCULOID TYPE 1 Leprotic reaction It occurs also in this type of cases 2 Muscular atrophies 3 Contractures and deformities 4 Necrosis of bones especially the small bones of the fingers and toes 5 Perforating ulcer 6 Ectropion of the lower eyelid corneal ulceration corneal opacities with subsequent blindness The ocular lesions are however less common in nerve leprosy 7 Leprous nerve abscess

Leprotic Reactions—These reactions are allergic in nature and often are precipitated as a result of vigorous treatment or in the course of the disease

A Signs of reaction in lepromatous leprosy—

1 Fever—short or prolonged 2 Acute lepra reaction or Erythema nodosum leprosum or Reaction anæmia complex It is a favourable sign In massive infection not only the skin mucosa and

peripheral nerves are affected but the hæmopoietic system is also involved particularly the bone marrow The patient is allergic to lepra bacilli 3 Appearance of erythematous nodules 4 Iriti 5 Lymphadenitis 6 Orchitis 7 Bone pain 8 Asthenia 9 High erythrocyte sedimentation rate (E S R)

B Signs of reaction in tuberculoid leprosy—1 Exacerbation of lesions 2 Œdema 3 Pain (neuralgic)

PROGNOSIS

The prognosis in a case of leprosy depends mainly on the following factors

1 Type and Stage of the Disease The progress of nerve leprosy is much slower than that of the skin type Patients belonging to the first group live much longer—20 30 years or even more The skin type runs a more acute course leading to a fatal issue usually in 8 10 years

2 General Resistance of the Individual If the patient has a high degree of resistance some of the earlier lesions especially of the nerve type may undergo a spontaneous resolution resulting in an apparent cure of the disease But if the natural resistance is low the disease runs a rapid course with development of wide spread lesions associated with febrile attacks and a fatal issue within 24 years is the usual result either due to the direct effects of leprosy or more commonly due to some intercurrent affection

3 Nature and Duration of Treatment With modern methods of treatment about two thirds of the early cases and one third of moderately advanced cases show marked improvement with disappearance of their lesions and are rendered non infective In markedly advanced cases the deformities atrophies and trophic lesions are obviously incurable The treatment should however be continued for years otherwise relapses are likely to occur Periodical observation with prompt resumption of treatment if necessary is essential to consolidate the stage of apparent cure

4 Intradermal Lepromin Test A strongly positive reaction indicates a favourable case (*Muir*)

DIAGNOSIS

An early diagnosis of leprosy is of very great importance from the point of view of treatment curative and preventive Ignorance shame and fear stand in the way of early diagnosis Ignorance of

the early manifestations on the part of medical men shame lest others would know of the presence of this loathsome disease and fear of loss of employment are responsible for the failure to detect the disease in its early and most amenable stage The first step of early diagnosis lies in the suspicion of the disease

EARLY DIAGNOSIS OF LEPROSY It is invariably made on clinical data of loss of sensation and by demonstration of *M lepræ* in biopsy material

DIAGNOSIS OF LEPROMATOUS TYPE *Clinical data* 1 Presence of a number of raised erythematous patches which are usually situated on the back buttocks or limbs and are very often not anæsthetic 2 Occasional presence of some small anæsthetic patches 3 Presence of some nodular thickening of the skin

Laboratory data Bacteriological examination for presence of *M lepræ*

1 Smears from the serous exudate obtained by scraping or puncturing the patch reveal the lepra bacilli 2 Snipped pieces of thickened skin taken from the lobule of the ear show large numbers of lepra bacilli 3 Snipped pieces even from unthickened ear lobules in infiltrative stage may show the bacilli 4 Nasal smear also yield positive results 5 Juice obtained on puncture of the lymph nodes may reveal bacilli

DIAGNOSIS OF TUBERCULOID TYPE *Clinical data* 1 Presence of light coloured or depigmented areas of skin which are anæsthetic to light touch 2 Thickening of a superficial cutaneous nerve in the neighbourhood of the depigmented areas 3 Loss of hair and absence of sweating over the affected areas

Laboratory data Bacteriological examination for presence of *M lepræ*

1 Sections from the erythematous margin of the skin may show a few bacilli 2 Sections of the skin from the centre of the anæsthetic patch almost always yield negative results 3 Examination of a nasal swab also shows no lepra bacilli

DIFFERENTIAL DIAGNOSIS

Infiltrated tuberculoid leprosy has to be differentiated from the following

1 NODULAR CUTANEOUS SYPHILIDE (*a*) History or evidences of a primary sore (*b*) Punched out circular ulcers (*c*) Positive

Wassermann reaction it is however not helpful as syphilis and leprosy may co exist Besides in a small percentage of cases of nodular leprosy the Wassermann reaction may be positive (*d*) Prompt response to antisyphilitic treatment

2 LUPUS VULGARIS (*a*) Presence of small apple jelly like nodules (*b*) Presence of normal sensation (*c*) Gross epidermal changes (*d*) Excessive scar formation

3 PSORIASIS (*a*) Presence of silvery scales over the lesions (*b*) Affection of the scalp which is rare in leprosy (*c*) Distribution of the lesions over the extensor surfaces of the limbs (*d*) Presence of normal sensation

4 DERMAL LEISHMANIASIS (*a*) History of kala azar in the past is usually present (*b*) Presence of normal sensation (*c*) Presence of *Leishmania donovani* in scrapings from the nodules

Tuberculoid macular leprosy may simulate the following

1 BIRTH MARK (*a*) Condition present from birth (*b*) Normal sensation present

2 LEUCODERMA (*a*) Presence of dead white flat patches surrounded by hyperpigmented skin (*b*) Absence of anæsthesia and thickening of cutaneous nerves (*c*) Characteristic distribution

3 LOCALISED SCLERODERMA (*a*) Obliteration of the natural furrows of the skin (*b*) Adherence to the underlying structures (*c*) Absence of anæsthesia

4 SEBORRHŒIC DERMATITIS (*a*) Presence of a scaly condition of the scalp (*b*) Presence of greasy scales over the patches (*c*) Presence of normal sensation (*d*) Response to treatment with sulphur

5 TINEA (*Ringworm*) (*a*) Presence of itching (*b*) Presence of mycelial filaments in the scrapings from the scaly borders of the patches

Neuritic Leprosy should be differentiated from

1 SYRINGOMYELIA (*a*) Dissociated sensory loss with preservation of sensation to light touch but loss of sensation to heat or cold and to pin prick (*b*) Segmental distribution of the sensory loss (*c*) Some spasticity of the lower limbs due to involvement of the pyramidal tracts (*d*) Presence of sweating over the anæsthetic areas (*e*) Scoliosis due to paralysis of the trunk muscles

2 PROGRESSIVE MUSCULAR ATROPHY (*a*) Presence of normal sensation (*b*) Presence of spasticity of the legs with evidences of a pyramidal lesion (*c*) Presence of fibrillation in the muscles

3 PERIPHERAL NEURITIS (*a*) Sensory loss and muscular wasting confined to the distribution of the affected nerve (*b*) Absence of thickening of the nerve trunk (*c*) No sensory loss over the trunk

4 CERVICAL RIB (*a*) Pain and numbness down one border of the arm or hand relieved by elevation of the shoulder girdle of the affected side (*b*) Muscular wasting and sensory loss which is often slight or absent correspond to the compressed cords of the brachial plexus and not to the distribution of the radial or ulnar nerve (*c*) No sensory loss in the trunk (*d*) Detection of the abnormal rib on x ray examination

5 RAYNAUD S DISEASE (*a*) History of recurrent attacks of vascular spasm affecting usually fingers and toes (*b*) Bilateral and symmetrical gangrene of the fingers and toes (*c*) Anæsthesia of the parts in which actual gangrene has occurred

Lepromatous macular leprosy Should be differentiated from 1 Erythema nodosum 2 Drug rash

Infiltrated lepromatous leprosy Should be differentiated from 1 Dermal leishmaniasis 2 Syphilis 3 Yaws

It is essential to remember that the presence of anæsthesia does not necessarily mean that the disease is leprosy Trauma is a great factor in the production of anæsthesia by causing injury to the nerve

TREATMENT

The main principles in the treatment of leprosy are to (*a*) raise the general resistance of the patient and maintain it at a high level by an adequate balanced diet regulated exercise suitable hygienic measures treatment of concomitant diseases and climatic change to a cool bracing climate (*b*) control the leprotic lesions by administration of chemotherapy (*c*) relieve distressing symptoms and (*d*) prevent and treat complications

GENERAL MANAGEMENT

It is essential to realise that the general health of the patient must be maintained at a high level of efficiency before a healing of the leprous lesions may be expected to occur A preliminary treatment of the

concomitant diseases such as malaria, syphilis, tuberculosis, hookworm disease, diabetes mellitus, dysentery and pyorrhœa alveolaris will raise the cure rate considerably.

REST AND EXERCISE. A regulation of rest and exercise is necessary. Walking, active outdoor games and drills are all very helpful in improving the general health.

CARE OF THE BOWELS. The bowels should be kept open regularly. Constipation and *diarrhœa should be avoided.*

DIET. It should consist mainly of bread, milk, meat, eggs, fish, butter and fresh green vegetables, so that it may be adequately balanced as regards the various proximate principles of food including mineral salts and vitamins, especially B_1 and C. We are of opinion that a diet *rich in potassium salts would prevent the allergic exacerbations* of the disease. Alcohol should be avoided.

SPECIFIC TREATMENT

1. SULPHONE DRUGS. Diamino diphenyl sulphone and certain derivatives of this compound act favourably, particularly in the lepromatous types of leprosy.

Promin (Glucose sulphone sodium).

Dose: 1·5 g a day. The initial dose of promin is 1 g intravenously daily, increased gradually by 1 g weekly up to a maximum of 5 g, *but most of the Indian patients do not stand more than* 3 g.

Diasone (Sulphoxone sodium). Each tablet—0·3 g.

Dose: *Oral*—0·3 g daily for 6 days—one day *off*; 0·6 g daily for 6 days—one day off; 0·9 g daily for 6 day—one day off. Maximum dose for adults should not exceed 0·9 g a day.

Solapsone or *Sulphetrone*. Oral and parenteral. Sulphetrone is best given parenterally, because when taken by mouth 80 per cent of the drug is excreted *via* fæces.

Parenteral—Injection sulphetrone fortis 2 c cm.—5 c cm. of 50 per cent. solution bi-weekly subcutaneously or intramuscularly.

Oral—One tablet (0·5 g.) daily—increasing by 0·5 g a week till 3 g a day is reached.

Dapsone or *Diaminodiphenylsulphone* (*D.D.S.*).

Dose: *Oral*—(i) 25 mg bi-weekly for two weeks.

(*ii*) *50 mg bi-weekly and increased by 25 mg* every two weeks till 100 mg bi-weekly is reached.

(iii) Raised by 100 mg a month till 300 mg

(iv) Then every day for 6 days—one day off

Continued for 1 to 2 years or more

Therapeutic results Clinical improvement is seen in the majority of cases The improvement consists in subsidence of infiltrated areas disappearance of small nodules decrease in size and softening of big nodules and subsidence of inflamed glands Remarkable results are seen in the treatment of ulcers nasal ocular and general which heal up quickly and do not recur Tendency to reaction is checked or reduced to a minimum Bacteriological improvement is also seen in many cases but this is neither so marked nor so uniform as clinical improvement About one fourth of the treated cases are rendered bacteriologically negative The limitation of the use of the drugs is that the treatment is very costly these are also useless in relieving nerve pains or curing nerve abscesses Other neural symptoms such as anaesthesia and deformities do not show any improvement

Toxic symptoms 1 Increase in lepra reaction 2 Rapid anaemia malaise weakness 3 Dermatitis (serious and distressing) 4 Hepatitis—Anorexia nausea vomiting jaundice 5 Psychosis

Anaemia of normocytic type may be produced and the severity is directly related to the dosage of the drug The anaemia however responds to the usual haematinics Patients on prolonged sulphone therapy usually has to be given iron liver yeast vitamin B etc whenever blood count tends to fall

2 CHAULMOOGRA AND HYDNOCARPUS OIL The Ayurvedic physicians have been using the chaulmoogra oil (expressed from the seeds of *Taraktogenos kurzii*) in the treatment of leprosy for thousands of years and they recommend two methods of treatment

(a) Daily rubbing of the oil over the whole body including the lesions and (b) Oral administration of the oil

Inspite of the introduction of sulphone drugs many experienced leprosy workers think that the chaulmoogra and hydnocarpus oils or their derivatives still have their place in treatment specially in tuberculoid type Combined sulphone and chaulmoogra treatment has also been advocated

Of the various preparations of chaulmoogra and hydnocarpus oil (from *Hydnocarpus wightiana* of South India and *Hydnocarpus*

anthelmintica of Siam and China) the following are extensively used and have given very good results

1 *Creosoted hydnocarpus oil* (containing 4 per cent creosote which acts as an antiseptic and analgesic) This is the preparation of choice

2 *Ethyl esters of whole hydnocarpus oil* This preparation causes marked pain on injection *Muir's E C O* mixture containing equal parts of ethyl esters of whole hydnocarpus oil and olive oil with 4 per cent. creosote is much less painful Iodised ethyl esters of the oil containing 1 per cent iodine are also less painful

3 *Sodium hydnocarpate (Alepol)* It is less irritating than other preparations of hydnocarpus and is comparatively painless and cheap

4 A combination of one or more of the preparations

Mode of action The injected oil causes a local irritation and *stimulates phagocytosis which leads to slow absorption of* granulomatous tissues and thus to the formation of antibodies It may also act as a protein shock therapy

Dose The initial dosage is 1 2 c cm which is increased at weekly intervals usually to 10 c cm Whenever possible a part of it is *injected* locally into the lesions or in and around affected area and the rest is given intramuscularly

Mode of administration The intradermal injection at the site of lesions is the method of choice The creosoted hydnocarpus oil is slightly warmed and injected intradermally by 5 10 punctures into a nodule or anæsthetic patch in doses of half a minim at each puncture each patch or nodule receiving an injection every 3-4 weeks Intramuscular injections of the oil are also given once a week into the gluteal muscles or into the outer aspects of the thighs Sites of intramuscular injections are changed each time to allow the absorption of the drug In absence of any local or general reactions the dose is gradually increased by ¼ c cm till the maximum dose is reached

Duration of treatment In early cases improvement sets in within 2 3 months of the commencement of treatment and the lesions usually clear up within a year requiring on an average about 100 injections In advanced cases the treatment has to be continued for 2 3 years The patient should be kept under observation for development of any signs of activity for 2 3 years after all symptoms have disappeared and the patient has been free from lepra bacilli

Signs of activity	Signs of inactivity
1 Increase of lesions	1 Arrest or regression of lesions
2 Erythema	2 No bacilli from scrapings of nasal mucous membrane and from several sites of skin at 3 monthly intervals—non infective It is quie cent if non infective for 6 month Arrested if quiescent for 2 years
3 Infiltration	
4 Increase of an esthesia	
5 Tenderness of nerves	
6 Presence of bacilli	

SYMPTOMATIC TREATMENT

LEPROTIC FEBRILE REACTIONS 1 ACTH and other corticosteroid are very helpful 2 Intravenous injections of 0 02 0 04 g of sodium or potassium antimonyl tartrate on alternate days till subsid nce of the reactionary fever 3 Calcium gluconate 10 per cent 10 c cm and glucose 25 per cent 250 c cm I V 4 Recently chlorpromazine in 25 50 mg dose has been used successfully in some cases

NEURALGIC PAINS 1 Aspirin gr 5 10 orally barbiturates opium or other analgesic drugs 2 Intramu cular injections of thiamine hydrochloride 10 50 mg daily for 2 3 weeks 3 Intramuscular injections of cobra venom once or twice weekly in graded doses of 1 20 mouse units relieves the pain in a large number of cases 4 Applications of diathermy—very helpful in relieving the nerve pains 5 In case of pain involving single nerve procaine may be injected into it

TREATMENT OF COMPLICATIONS

TROPHIC ULCERS (a) Surgical measures of cleanliness including removal of dead bone and necrotic skin Local application of olive oil or hydnocarpus oil dressings Penicillin injections if secondary infections present (d) Protein shock therapy with (i) Intravenous injections of T A B vaccines in graduated doses of 25 100 millions (ii) Intramuscular injections of 10 c cm of milk (c) Ultraviol t irradiation (d) Deep x ray exposures (c) Periarterial sympathectomy (f) Avoid trauma

CONTRACTURES AND DEFORMITIES (a) Appropriate surgical measures uch as nerve stretching and various pla tic operations (b) Ma sage pa sive and active movements

PREVENTIVE MEASURES

The preventive measures against leprosy consist of the following

GENERAL PROPHYLAXIS 1 Compulsory notification Survey of hidden cases

2 Early recognition of cases by a careful clinical and bacteriological examination of all contacts with leprous patients especially the school children in leprous areas every six months for a period of five years

3 Prompt and efficien treatment of non infective cases at the out patient clinics especially established for the purpose

4 Isolation of advanced infective cases especially from children under ten years and their removal to leper colonies or special leper hospitals where suitable arrangements should be made for their living occupation and treatment The advanced mutilated cases of nerve leprosy are not infective and hence they need not be isolated The segregation should be carried out on humanitarian principles Any rigid and compulsory method of segregation of all lepers is very likely to lead to a wilful concealment of the disease Thus recognition of early curable cases will not be possible

5 Removal of all children immediately after birth from their infective leprous parents to the homes of their healthy relatives who will bring them up till they reach the adult life

6 Establishment of separate schools for the education of leprous children

7 Educative propaganda amongst the medical and lay public on the causation mode of infection spread and prevention of the disease

PERSONAL PROPHYLAXIS 1 In cases of home isolation the healthy persons should avoid prolonged contact with the infectious leprous patient and should not use his articles

2 The attendants should use rubber gloves during dressing the wounds of leprous patients

3 The contacts should maintain an efficient general health by means of suitable nourishing diet fresh air and exercise

L K G

	Lepromatous	Tuberculoid	Dimorphous
A Macular lesion			
	Lepromatous macular	Maculotuberculoid (Macula anæsthetica)	Dimorphous macular (Indeterminate)
Number	Multiple	Single or multiple	Single at first then multiple
Size	Small	Large	Large and small
Distribution	Symmetrical	Asymmetrical	Symmetrical
Site	Scattered all over the body	Common in face extremities buttocks and scapular region	Scattered all over the body
Lesion	—	Hypopigmented	—
Edge	Not well marked edge	Edges not raised but well defined to clearly demarcate healthy from the affected skin	Edges definite in large macules only
Surface	Smooth erythematous	Dry anhydrotic rough	Wrinkled
Sensation	No loss	Loss of tactile sensation	Loss of sensation in large macules only
Associated features	—	Enlargement of peripheral nerves	
Bacilli	Usually positive	Usually negative	Usually negative
Lepromin reaction *	Negative	Strongly positive	Variable
B Infiltrated lesion			
	Infiltrated lepromatous leprosy	Infiltrated tuberculoid leprosy	Infiltrated dimorphous leprosy (Borderline)
Nature	i Diffuse ii Infiltrated (an advanced stage of macular leprosy) iii Nodular (Ear fingers genitals) Soft in feel	Benign Stable Large	
Distribution	Sites of macules	Asymmetrical Outer aspect of extremities face scapulæ buttocks	
Sensation	—	Gross asymmetrical sensory loss	
Nerve	—	Enlarged abscess formation frequent	
Bacilli	Nasal swab positive	Negative	
Lepromin reaction	Negative	Strongly positive	

C Neuritic (Anæsthetic) lesion

Signs Anæsthesia, nerve enlargement muscular paralysis trophic changes The polyneuritic variety is the most mutilating form

* The lepromin reaction indicates the degree of immunity

CHAPTER V

PLAGUE

[Black Death Pestis]

DEFINITION

Plague is a specific infectious disease caused by the *Pasteurella pestis* It is clinically characterised by high fever septicæmia acute inflammation of the lymph glands and rarely of the lungs Mortality is high

HISTORY

The disease can be traced to have occurred as early as 542 A D in an epidemic form in Egypt In 1664 A D one seventh of London's inhabitants died of plague In 1894 an epidemic broke out in Hongkong where Kitasato and Yersin isolated the *Past pestis* from the human patients Next it spread by the sea routes to Japan India and Egypt in 1896 Gradually the disease spread to the Philippines and South America

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is widely prevalent At present it is endemic in the South West of China Japan the Philippines Africa and parts of South America But it has been chiefly endemic in India since the most severe epidemic in 1907 which caused the death of about one million and a half people It is perhaps always present in some parts of India such as the States of Bombay Uttar Pradesh and Bihar though the incidence varies from year to year according to the climatic and other conditions

The incidence of the disease is however on the decline in recent years Madras certain places in East Pakistan such as Dacca and Assam are free from plague This immunity of certain places is due to prevalence of rat fleas such as *Xenopsylla astia* which are poor carriers of plague as in Madras and incidence of floods during the rains and consequent scarcity of rats as in East Pakistan

AGE SEX AND RACE INCIDENCE Plague occurs at all ages Both sexes are almost equally susceptible The females show a slight preponderance because they live more inside the house All races are equally liable

OCCUPATION It has little or no influence

SEASONAL PREVALENCE The seasonal occurrence of plague in India varies in different places according to the temperature and humidity of the atmosphere and prevalence of the rat fleas An atmospheric temperature of 50° 80 F associated with a certain amount of humidity favours the incidence of plague In temperate climates fleas are most numerous in summer and autumn when bubonic plague is most prevalent Very high temperature and a very dry atmosphere with low humidity are unfavourable conditions for the life of the rat fleas and hence a sudden decline in the incidence of plague is noticed with the onset of hot weather A very low atmospheric temperature is also inimical to the fleas The incidence of pneumonic plague is not influenced by atmospheric conditions as it is not caused by the rat fleas

PREDISPOSING FACTORS 1 Atmospheric conditions suitable to the life of the rat fleas

2 Prevalence of rats and rat fleas in the locality

3 Housing conditions which favour the harbouring of rats Houses which are closely aggregated and have thick mud walls mud floors and store rooms of grains harbour numerous rats and are thus more liable to be affected than rat proof brick built houses

CAUSATIVE ORGANISM The causative organism discovered by Kitasato and Yersin is known as *Pasteurella pestis* (*Bacillus pestis*) It is a thick small non motile bacillus measuring 1 2 *microns* in length and 0 5 0 7 *micron* in breadth It is a gram negative organism which stains more deeply at its two rounded ends showing the characteristic bipolar staining It can easily be cultured within 24 to 48 hours in suitable media such as broth agar and blood serum

MODE OF INFECTION

1 INOCULATION BY INFECTED RAT FLEAS Plague occurs primarily as an epizootic in rats and other rodents such as rabbit guinea pig monkey mouse ground squirrel *Epidemics in rats invariably occur 2 3 weeks prior to the outbreak of plague in human population* Two varieties of rats viz the grey rat (*Rattus norvegicus*) and black rat (*Rattus rattus*) are most commonly affected The grey rat is smaller but stouter greyish brown in colour has a stout tail and is found in drains and grain stores whereas the black rat is longer but slender dark brown in colour has a tail longer than the body and is found mostly in houses *The epizootic at first occurs among the sewer* rats and then spread by means of the infected fleas to the house rats

According to the Indian Plague Commission the disease is carried from one rat to another by the bites of rat fleas which have fed on the blood of the diseased rats Their view is based on the experimental fact that healthy rats kept in most intimate contact with plague infected rats from the body of which all fleas have previously been removed never contract plague Physical contact with the diseased rats or even close proximity to them is not necessary for the occurrence of the infection as the disease is conveyed by the rat fleas The rat flea chiefly responsible for the transmission of plague in India is *Xenopsylla cheopis* which acts as the most efficient carrier of the plague bacillus because there is more rapid multiplication of *Past pestis* in the œsophagus and hence earlier blocking of the same than in other fleas In Europe and North America *Nosopsyllus fasciatus* is the common carrier The rat flea feeding on the blood of an infected rat sucks a large number of plague bacilli with the blood which forms a gelatinous clot in the œsophagus where bacilli multiply and retain their virulence upto 3 6 weeks after which they pass out with the fæces Under suitable atmospheric conditions associated with a moderate temperature and humidity the infected fleas may live as long as two months When the infected rats die the rat fleas leave their cold bodies and invade the healthy rats When the rats get scarce and other suitable victims are not available they begin to bite man usually in the bare feet and legs or in the hands especially of sweepers while removing the dead rats which are still warm During biting the infected flea whose œsophagus has already been partially obstructed by the gelatinous blood clot containing almost a pure culture of plague bacilli as a result of it previous feeding on the blood of diseased rats cannot suck in blood and so regurgitates part of the blood clot into the wound and thus inoculates it with plague bacilli During the act of sucking the rat flea may deposit on the surface of the body its fæces containing a large number of plague bacilli which may enter the body through any existing breach of skin in that area The bacilli may also be deposited on the body by the contaminated mandibles (mouth parts) of the flea This contaminative method of infection is however not a common one

2 Droplet Infection It is the method of infection in pneumonic plague where persons coming in contact with the patient are infected by droplets of sputum carrying myriads of bacilli during coughing or sneezing Fortunately however pneumonic plague is rare in India constituting about 3 per cent of all cases of plague

3 Accidental Inoculation This method of infection which

is very rare is reported to have occurred amongst medical men during autopsies or dissections of dead bodies of plague victims

MODE OF SPREAD

The disease spreads from place to place in the following ways

1 The infected individual carries the disease during the incubation period when he travels from one locality to another Once the infected person develops an attack of plague he does not communicate the disease directly to another person (except in the pneumonic type) About a fortnight later plague breaks out amongst the rats through infection by fleas which had bitten the first patient A few days later people living in the same house or in the neighbouring houses are attacked and the disease begins to spread throughout the locality

The infection may sometimes be transmitted from one patient to another by the human fleas (*Pulex irritans*) without passage through the rats (*Wu Lien Teh*)

2 Healthy individuals may carry infected rat fleas on their persons or in their baggages from one place to another though they themselves may escape the infection

3 Infected rats may migrate during the incubation period and carry the disease to the neighbouring places The infection may spread to the different countries by the sea route through infected rats or rat fleas being carried in grain bags on ships Infected rats suffering from a chronic form of plague characterised by chronic buboes and abscesses in the spleen may carry over the infection from one season to another

Once an epidemic breaks out in a large town it may continue for months or even years till the development of immunity in the rat population

PATHOLOGY

BUBONIC TYPE From the site of inoculation the plague bacilli are usually carried to the lymph nodes draining that area and produce inflammation and enlargement of the glands forming primary buboes The sub-inguinal glands frequently and the axillary and cervical ones to a less extent are markedly swollen and soft due to oedema and hæmorrhages in the periglandular tissues Hæmorrhages and necrosis may also be present in many of these glands Other lymph nodes of the body may be involved secondarily and show moderate enlargement as a result of congestion

When the infecting plague bacilli are of low virulence and the resistance of the patient is high a primary vesicle appears at the site of the flea bite in about 5 per cent of cases of bubonic plague Other local lesions such as carbuncles pustules may also appear Such lesions are usually found towards the end of the epidemic

SEPTICÆMIC TYPE. If the bacilli are virulent and the resistance of the individual low they rapidly invade the blood stream *via* the lymphatics and lymph nodes without forming any buboes and cause a septicæmia There is congestion of the various organs of the body The endotoxins liberated by the bacilli damage the endothelial cells of the blood and lymph vessels and give rise to hæmorrhages in the skin mucous membranes and serous sacs The skin may show multiple petechial spots the occurrence of which justifies the old name *Black Death* applied to the disease Congestion and hæmorrhages may be found in the peritoneum pleuræ pericardium meninges and the brain. Similar changes may occur in the stomach bowels and urinary tract

The heart muscle shows evidence of fatty degeneration The right side of the heart is dilated and the large veins are found distended with fluid blood Liver and kidneys show intense congestion with cloudy swelling and fatty changes The spleen is congested and usually enlarged

PNEUMONIC TYPE In the pneumonic type which occurs in about 3 per cent of cases of bubonic or septicæmic plague the bacilli make their way to the lungs which show usually a patchy broncho pneumonic and sometimes a lobar consolidation associated with hæmorrhages and œdema of the interstitial tissues The alveolar exudate is hæmorrhagic but practically free from fibrin The sputum is profuse thin watery and blood stained and contains millions of plague bacilli The pleural sacs contain blood stained serum The bronchial glands are enlarged and hæmorrhagic The larynx and trachea may show intense congestion There is no formation of buboes nor any enlargement of the lymph nodes

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually 3 4 days though it may vary from 2 10 days

MODE OF ONSET The onset is usually sudden though some case may show the following prodromal symptoms

(*a*) Lassitude and mental depression (*b*) Pains in the back and limbs and especially over the groins the sites of the future bubo (*c*) Chilly sensations (*d*) Loss of appetite

With the onset of the disease there is a rapid rise of temperature associated with rigor up to 103° – 104°F or even more The temperature may be high continued or remittent The patient has an anxious appearance and looks extremely ill even on the first or second day of the disease The following signs and symptoms of intense toxæmia soon supervene

(*a*) *General*—flushed face with injected conjunctivæ staring eyes with dilated pupils

(*b*) *Nervous*—headache restlessness mental apathy staggering gait dysarthria mental confusion delirium subsultus tendinum

(*c*) *Alimentary*—dry and heavily coated tongue nausea and vomiting Both the liver and spleen are enlarged

(*d*) *Circulatory*—rapid and thready pulse with a weak first sound of the heart

(*e*) *Urinary*—scanty urine with slight albumin

(*f*) *Hæmorrhagic manifestations*—hæmorrhages into skin from nose stomach bowels lungs and kidneys may occur

The subsequent course of the disease may conveniently be described under the following clinical types

CLINICAL TYPES

1 BUBONIC PLAGUE It is the commonest and most easily recognisable type in most epidemics Perhaps on the very first day the patient who has high fever associated with headache and backache complains of pain and tenderness in the groin and in most cases the characteristic primary bubo appears on the second or third day The glands in the groins are affected in 60 70 per cent of cases axillary glands in 15 20 per cent and sub maxillary in some The glands in the groins are most frequently affected as the rat fleas bite more often on the feet or legs than on any other part of the body Usually there appears a single bubo though in some cases it may appear on both sides at the same time The bubo has usually the size of an egg or may be larger It is often so painful and tender that the patient keeps the thigh of the affected side flexed on the abdomen On palpation the bubo feels soft and boggy due to the periglandular œdema which obscures the underlying individual glands which are enlarged and discrete Secondary buboes develop later

The blood examination shows in the early stages (*a*) moderate leucocytosis 15 000 20 000 white cells per c mm (*b*) marked polymor

phonuclear leucocytosis which is very characteristic (b) normal o increased red cell count due to dehydration and (d) plague bacilli on blood culture Later on there may be granulocytosis with slight normocytic anæmia

In *mild cases* the constitutional symptoms begin to abate after the appearance of the bubo the temperature gradually decline the buboes may subside and convalescence usually begins on the 6th to 10th day though in some cases it may be delayed till the 1 th to 20th day But in many cases the buboes suppurate during the second week and may burst or require incision Burst or incised buboes may take weeks or months to heal The pus from the buboes shows not only the plague bacilli but also pyogenic organisms such as sterptococci and staphylococci

In *severe cases* the constitutional symptoms are aggravated and toxæmic symptoms as described previously appear on the 3rd to 4th day of the disease The temperature is usually high but may be low under the burden of an overwhelming toxæmia Petechial eruption appear on the body Respirations are rapid and shallow broncho-pneumonia develops as a result of infection by secondary organisms or by plague bacilli themselves The patient gradually passes into a typhoid like state associated with delirium and coma Death occurs from heart failure due to severe intoxication on the 4th or 5th day of the disease

2 SEPTICÆMIC PLAGUE It is comparatively rare In this type toxæmic manifestations are more pronounced The patient looks very ill and prostrated from the very onset and may be in a highly delirious or comatose condition The temperature is often low due to the overwhelming toxæmia Buboes are absent but the lymphatic glands all over the body are slightly enlarged Spleen may be palpable Hœmorrhages into the skin and from mucous membranes are frequently seen The white cell count rises as high as 50 000 60 000 per c.mm or even more Blood shows plague bacilli in direct smear and also on culture Death occurs on the first to third day

3 PNEUMONIC PLAGUE This type which is the most fatal of all is fortunately rather uncommon in India It may be primary but is invariably secondary to a bubonic or septicæmic case of plague The characteristic features are (1) the sudden onset with rigors pain in the chest and the limbs and high fever (2) cough and cyanosis with rapid shallow respirations (3) expectoration of profuse watery blood tinged dark prune juice coloured sputum containing enormous number

of plague bacilli (4) scattered deep seated patches of bronchopneumonia with scanty physical signs in the lungs (5) absence of localised or generalised enlargement of lymph glands and (6) occurrence of marked delirium and death from cardiac failure usually on the third to fourth day

4 CELLULO CUTANEOUS TYPE It is characterised by the appearance of carbuncle like lesions in the skin surrounded by vesicles or pustules simulating anthrax The fluid discharge from the lesions however contains almost a pure culture of plague bacilli Such lesions usually occur in the early or later stages of the disease The prognosis in these cases is often good because of the low virulence of the infecting organisms though in some cases the lesions may be multiple and may slough leading to extensive gangrene and death

5 AMBULATORY OR ABORTIVE TYPE (*P stis minor*) This is a very mild type of bubonic plague which is rare It is characterised by slight fever some enlargement of the lymph glands and little or no constitutional disturbance The diagnosis of such cases is difficult as the patients are usually up and about and the enlarged glands which occasionally suppurate are often mistaken for lympho granuloma inguinale The presence of numerous plague bacilli in the juice obtained by gland puncture however clinches the diagnosis

6 INTESTINAL TYPE It is very rare and characterised by vomiting and frequent passage of liquid stools which are fæculent and blood stained

7 CEREBRAL TYPE It is characterised by a predominance of cerebral symptoms such as delirium convulsions and coma Thus it may closely simulate cerebral malaria

Other rare types only occasionally described in literature include vesicular or varioloid type and anginal or tonsillar type

COMPLICATIONS

1 Cardiac failure 2 Bronchopneumonia and pneumonia 3 Septicæmia 4 Delirium and coma 5 Hæmorrhages into the skin and from mucous membranes 6 Suppuration of the buboes 7 Carbuncle and cellulitis 8 Parotitis occasionally 9 Abortion in pregnant women—almost invariable 10 Meningitis occasionally

PROGNOSIS

In pneumonic type the disease is almost always fatal death occurring usually within 1-4 days of the onset In septicæmic type of plague

the prognosis is very grave and death occurs in majority on the 4th or 5th day of the disease In moderately severe cases of bubonic plague with a negative blood culture death rate varies from 10 30 per cent. The prognosis is considerably influenced by good nursing and better hygienic conditions Sudden onset of fever high continued and prolonged temperature rapid pulse delirium and marked prostration from the very on et are all unfavourable signs In mild cases of bubonic type showing suppurated buboes carbuncles or pustules the patients generally recover but the convalescence is very slow because the wounds are indolent and take a long time to heal The use of the modern chemotherapeutic drugs has however improved the progno i considerably

DIAGNOSIS

During an epidemic the diagnosis can be easily made from the following data

BUBONIC PLAGUE *Clinical data* 1 Occurrence of death among the rats of the locality 2 Sudden onset of fever with rapidly developing toxemia and stupor 3 Enlargement and tenderness of the lymph glands

Laboratory data 1 Microscopical examination—Examination of smears from the juice obtained by glandpuncture shows plague bacilli with characteristic bipolar staining

2 Cultural examination—(*a*) Culture of blood 10 c cm of blood should be taken in a small flask containing 20 c cm normal saline and 1 per cent sodium citrate (*b*) Culture of material from the affected gland

3 Inoculation in animals such as guineapigs and white rats—The material from the gland juice sputum blood cultures is rubbed into the cleanly shaven skin of the abdomen of the animal which dies within 3 5 days and shows at necropsy the typical lesions of rodent plague The inoculation experiment on white rats is the crucial test for the identification of plague bacilli

4 Agglutination reaction—The te t for the presence of serum agglutinins is of no value in diagnosis or identification of the bacilli because the agglutinins appear in the serum of the patients after a fortnight from the onset of the disease and moreover the plague bacilli frequently show auto agglutination

SEPTICEMIC PLAGUE It is very difficult to diagnose this type of plague in the beginning of an outbreak and in absence of bubonic cases

Clinical data 1 Occurrence of death amongst the rats of the locality 2 History of occurrence of a number of rapidly fatal cases of similar fever in the locality 3 Rapid onset of severe toxæmia

Laboratory data 1 Presence of plague bacilli in the blood smear in about 17 per cent of cases 2 Positive blood culture

PNEUMONIC PLAGUE *Clinical data* 1 Onset of high fever with marked prostration dyspnœa and cyanosis 2 Presence of scanty physical signs in the lungs 3 Thin watery blood stained sputum 5 Occurrence of several cases in the family

Laboratory data 1 Smear examination of the sputum shows numerous plague bacilli 2 Culture of sputum and blood reveals plague bacilli

DIFFERENTIAL DIAGNOSIS

Bubonic plague has to be differentiated from the following

FILARIAL LYMPHADENITIS 1 History of repeated attacks of similar fever with adenitis 2 Less toxæmia 3 Presence of signs of lymphangitis 4 Presence of microfilariæ in blood

CLIMATIC BUBO (*Lymphogranuloma inguinale*) 1 Chronic affection with a gradual onset 2 Less constitutional symptoms 3 Absence of the characteristic diffuse swelling and the exquisite tenderness as seen in a plague bubo 4 Examination of blood or gland puncture material before suppuration does not show any organism 5 Positive intradermal test of Frei

PYOGENIC LYMPHADENITIS 1 Presence of an obvious source of sepsis in the foot or leg

SYPHILITIC BUBO 1 History of an exposure to syphilitic infection 2 Presence of a penile sore 3 Presence of discrete and almost painless enlargement of the lymph glands 4 Positive Wassermann reaction

RAT BITE FEVER 1 History of a bite by a rat or sometimes by a cat 2 History of recurrent attacks of fever 3 Presence of an erythematous or macular rash 4 Less toxæmia 5 Occasional presence of *Spirillum minus* in the peripheral blood 6 Detection of *Spirillum minus* on inoculation of white rats with human blood

Septicæmic plague should be differentiated from cerebral malaria typhoid fever typhus fever pneumococcal streptococcal or staphylococcal septicæmia Blood culture is the most certain and reliable method of diagnosis of the nature of septicæmia

Pneumonic plague is differentiated from pneumococcal pneumonia by the following

1 Early appearance of severe prostration associated with scanty physical signs in the lungs 2 Presence of thin watery and blood stained sputum 3 Early appearance of a pleural effusion 4 Presence of plague bacilli in the sputum in smear and culture

Cellulo cutaneous type of plague may be differentiated from anthrax by the following

Presence of *P pestis* in culture of the exudate from the small vesicles

GENERAL TREATMENT

The patient should be put to bed at once The room should be clean well lighted and ventilated and should contain no unnecessary furniture No visitors or relatives should unnecessarily be allowed into the room Good nursing is essential The nurse and doctors should use gloves and wear masks of muslin especially in dealing with pneumonic cases which should better be kept in the verandah Sputum clothing and bedding are highly infectious and should be burnt

DIET Light nourishing liquid diet is desirable and milk whole or skimmed should be the chief ingredient supplemented with easily assimilable carbohydrates Patients should not be under fed as it is a very exhausting disease

CONVALESCENCE The patient should be allowed to sit up at first for a few minutes and then for a few hours in the day provided there is no undue acceleration of the pulse rate Sudden death from cardiac failure may occur unless great caution is exercised

SPECIFIC TREATMENT

ANTIBIOTICS 1 *Streptomycin* has proved to be very effective in the recent epidemic The usual dose recommended is 1 g intramuscularly immediately followed by ½ 1 g every 6 hours for 6 to 8 days In severely toxic cases combined treatment with sulphadiazine intravenously and streptomycin intramuscularly is of absolute necessity

2 *Sulphonamides* have been of great value in protecting and treating rodents such as rats and mice experimentally infected with *P pestis* (Schutze) In an average case 2 g sulphadiazine sodium intravenously immediately followed by 1 g 4 hourly intravenously brings about clinical and bacteriological cure within 2 3 days The drug must be continued for one week 6 g a day by oral route

SYMPTOMATIC TREATMENT

HIGH TEMPERATURE 1 Application of ice bags to the head 2 Cold or tepid sponging 3 Ice cradling 4 Iced rectal saline 5 Withholding of depressant antipyretic drugs

VOMITING 1 Calomel and chloretone in fractional doses 2 Cracked pieces of ice to suck 3 Hypodermic injections of gr 1/100 of atropine sulphate repeated if necessary 4 Largactil 25 50 mg

PAIN RESTLESSNESS AND SLEEPLESSNESS 1 Administration of sedative drugs such as bromide and chloral hydrate 2 Hypodermic injection of morphine sulphate gr ¼ is perhaps the best method of relieving pain and promoting sleep

CIRCULATORY COLLAPSE 1 Administration of 1 pint of 5 per cent glucose with normal saline solution by the intravenous route to be repeated once or twice a day 2 Injection of nikethamide nor adrenaline and other peripheral stimulant 6 hourly

BUBO 1 Application of ichthyol glycerine and belladonna 2 Hot fomentations 3 Incision in case of suppuration may be necessary

PREVENTIVE MEASURES

It is essential to direct the attention to prevention which is more important than curative treatment

GENERAL PROPHYLAXIS 1 *Compulsory early notification*

2 *Quarantine measure* Examination of passengers leaving infected areas by land or water routes should be enforced Infected people should not be permitted to travel All contacts should be placed in quarantine for at least 10 days as some of them may be travelling during the incubation period of the disease

3 *Isolation of the patient*

4 *Disinfection of the infected house and articles and clothes used by the patient* The discharges from the glands and vesicles sputum stool and urine all being highly infective should very cautiously be disposed of or preferably burnt

5 *Destruction of rat fleas* Dieldrin or DDT and pyrethrum used as sprays or dusting powders are very effective in exterminating the flea

6 *Rat elimination* (a) Adoption of measures which lessen the amount of food water and shelter for rats and thus reduce their

number (*b*) Building of rat proof houses with cemented floors and brick walls though this alone is not sufficient to get rid of the rats (*c*) Protection of stores of grains and food from the depredation of rats (*d*) Protection of ships with rat guards

7 *Rat destruction* (*a*) Trapping

(*b*) Poisoning by preparations of arsenic and phosphorus and barium carbonate The last is decidedly the best rat poison The baits which are made from a firm paste containing 3 grains of barium carbonate mixed with about 4 5 grains of flour are laid in places accessible to rats Precautions should however be taken that children may not get access to these baits

(*c*) Fumigation The above methods of rat destruction by trapping and poisoning are now a days being replaced by cyanide fumigation of rats and fleas in burrows and stores Calcid available as tablets which have a high cyanide content is superior to calcium cyanide A dust especially in fumigation of premises which cannot be completely sealed (*Sokhey et al*)

8 *Evacuation of infected houses and localities* The most essential measure is to leave the houses and the locality at the very onset of a large epidemic The whole population of the affected place must leave at the same time and live well outside the infected area in temporarily built huts and camps till the disease dies out The infected houses should be thoroughly disinfected before they come back The floor of the room and wall upto 2 3 feet should be thoroughly rinsed with kerosene oil The cracks and crevices in the floor and walls which harbour the rat fleas should be particularly attended to The rooms may also be disinfected by sulphur fume solutions of perchloride of mercury and other chemicals but it is very doubtful if these agents ever reach the infected rats and rat fleas

PERSONAL PROPHYLAXIS 1 Inoculation of all contacts For this purpose Haffkine s antiplague prophylactic vaccine is used in India Recently certain modification has been introduced in the preparation of the vaccine The organisms are grown for 48 hours at 37°C on agar and a saline suspension is made The bacilli are killed by heating at 54°C for 15 minutes 0 5 per cent phenol is added to the killed bacilli and the vaccine is standardised to contain 1000 million organisms per c cm The vaccine is best given in two doses 0 5 to 1 c cm for the first dose followed by 1 to 2 c cm a week later During emergency a single dose of 2 c cm may be given Reaction with the

recent vaccine is much less than the original vaccine The protective value of this vaccine is also said to be better than that of the original old Haffkine's vaccine

Though the inoculation may not confer an absolute protection yet it undoubtedly produces a certain immunity which lasts from six months to eight months The result of inoculation is satisfactory in as much as it causes about 80 per cent reduction in the incidence and mortality of the disease amongst the inoculated persons

Lately inoculation on a large scale has been carried out in Java and Madagascar by vaccines made from living avirulent strains of *P pestis* (*E V strain*) There have been few or no untoward effects and the results are satisfactory Outside India this vaccine is used in preference to the Haffkine's vaccine

2 Wearing of thick flea proof socks and boots and gowns by attendants doctors and nurses

3 Use of rubber gloves face masks and goggles during attendance especially in case of pneumonic plague

4 Avoidance of visits to the plague stricken houses or localities especially at night when the fleas bite most

5 Chemoprophylaxis of contact with 1 g of streptomycin daily for 5 days

A M

SECTION IV DISEASES CAUSED BY SPIROCHAETES

CHAPTER I

LEPTOSPIROSIS

DEFINITION

It is a group of febrile illnesses with constitutional symptoms marked prostration and usually with neutrophilic leucocytosis Jaundice may or may not be present The classical Weil's strain is *Leptospira icterohæmorrhagiæ* Other strains are *L hebdomadis* which primarily infects the field vole and causes in man the seven days fever of Japan *L canicola* commonly affects dogs from which man acquires infection There are a number of other strains *e g* *L autumnalis* of Japan *L pyrogenes* of East Indies *L grippotyphosa* of Europe and Andaman etc

WEIL'S DISEASE

[Spirochætosis icterohæmorrhagica Spirochætal jaundice]

It is an acute infectious febrile disease occurring epidemically or sporadically caused by *Leptospira icterohæmorrhagiæ* and clinically characterised by fever jaundice enlargement of the liver and occasionally of the spleen nephritis and hæmorrhages into the skin and from the mucous membranes in severe cases

ETIOLOGY

Geographical Distribution The disease has a wide spread distribution It is chiefly prevalent in Japan but outbreaks have occurred in Queensland the Malaya States the Dutch East Indies and the Andamans Its occurrence has been reported from different parts of India such as Bombay, Kashmir, South India and Calcutta In Europe the disease occurs frequently in Holland It also occurs in the British Isles Germany France Italy North African Coast and the Mediterranean areas It is endemic in West Africa and South America Cases have also occurred in the United States of America

Seasonal Prevalence In Japan the highest incidence is in September to November In Europe especially in Holland the disease occurs chiefly in the summer months In the Andamans epidemics break out during the monsoon In Calcutta cases are seen in the rainy season and also in winter

Age and Sex Incidence The disease may occur at any age

though adults are most frequently affected Children may be infected by bathing in polluted and stagnant water of rivers pools or even swimming baths Men are especially liable to the infection because of their out door occupations The incidence in fish cleaners is equally distributed between the two sexes

OCCUPATION Weil s disease may be definitely considered as an occupational disease It occurs amongst persons who are exposed by virtue of their occupation to wet soil or stagnant water polluted with the urine of infected rats Hence the disease is frequently seen amongst workers in coal mines sewers rice fields sugar cane fields and fi heries Dairy farmers and butchers are also liable to be affected Cooks *durwans* (guards) and those who live in the ground floors of old houses are also susceptible because of the chance of contamination of their food and drink with the urine of infected rat

CAUSATIVE ORGANISM The disease i cau ed by *L ptospira icterohæmorrhagiæ* which was discovered by Inada and Ido in 1915 during an epidemic in Japan It is an actively motile piral filament about 5 12 *microns* long The two ends taper to points It is present in the blood of the patient before the sixth day in the urine after the tenth day It is also present in the sputum and spinal fluid

Sources of infection—The pathogenic lepto piræ are parasites of animals like rats dogs and pigs

MODE OF INFECTION

The organism gains entrance to the human body through obvious or minute abrasions in the skin or mucous membranes especially of the nose and conjunctive during contact with the wet soil slime or tagnant water contaminated with the urine of rats infected with leptospire Other modes of infection such as drinking of contaminated water bites by infected rats or accidental inoculation with living cultures of the organism have been reported from time to time The incidence of leptospiral infection in rats of any locality is not nece arily pro portionate to that of human lepto pirosis In New York with 60 per cent of infected rat there are only a few records of lepto piral infection in man whereas in Calcutta with about 2 per cent of rat infection human lepto piro is is more frequent

PATHOLOGY

On entry into the body tis ues the organi ms invade the blood stream multiply rapidly and in cour e of a week locali ation occurs in various internal organs e pecially the liver and the kidneys

LIVER It is always enlarged and congested Groups of hepatic cells may show evidences of necrosis and hyaline degeneration Hepatic damage is often minimal and inconstant The liver may however show lymphocytic infiltration around the portal tract as in the late stage of acute infective hepatitis No obstruction to the bile ducts has been observed Evidence of regeneration is the outstanding feature *L icterohæmorrhagiæ* may be shown in large numbers in the hepatic cells by Levaditi s method of silver nitrate impregnation

GALL BLADDER It may be distended with dark viscid bile

SPLEEN It is congested soft and diffluent Occasionally enlarged

KIDNEYS The kidneys are congested and swollen Hæmorrhages may occur in the intertubular tissues Microscopic examination reveals uniform and characteristic changes of interstitial nephritis and degeneration of the cells of the convoluted tubules Glomeruli are least affected Leptospiræ in large numbers may be demonstrated in the tubules and glomeruli The lesions present the features of lower nephron nephrosis (distal tubular necrosis)

STOMACH AND DUODENUM They may show petechiæ in the submucous tissues

LUNGS AND PLEURE These may show patches of hæmorrhage

BONE MARROW It shows proliferation of myelocytes deposition of pigment in the macrophage cells and diminished activity of the hæmopoietic system

LYMPH NODES May be enlarged The inguinal cervical and epitrochlear glands are frequently affected Enlargement is due to a marked proliferation of the endothelial cells

MUSCLES Show punctate hæmorrhages The calf muscle are very commonly affected

BLOOD The red cells are diminished to a certain extent A count of 2 5 3 millions per c mm is common The hæmoglobin is proportionately reduced There is a leucocytosis of 12 000 25 000 per c mm The platelets may be reduced to as low as 10 000 per c mm The coagulation time of the blood may be prolonged to 20 minutes The sedimentation rate is raised

CLINICAL MANIFESTATIONS

INCUBATION PERIOD Usually it is 5 12 days

MODE OF ONSET The on et is usually sudden associated with

moderate or high temperature severe frontal headache backache and pains in the joints and muscles rigor with occasional epigastric pain vomiting and diarrhœa

GENERAL APPEARANCE The face is flushed the eyes are pink coloured because of intense congestion due to dilatation of episcleral vessels The patient appears to be extremely weak and prostrated Jaundice appears by the 3rd to 4th day

FEVER The temperature rises on the 1st day to 102° 103°F and is remittent in character The maximum is reached on the 3rd to 5th day (Fig 31) when jaundice appears in about 60 per cent cases and the temperature falls by crisis or lysis reaching the normal level by 7th to 10th day though in mild cases the febrile period may not lasts for more than 5 days

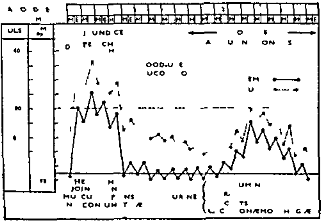


FIG 31 Temperature chart of Weil's disease showing the late appearance of relative bradycardia and secondary fever

Usually there is one pkll of fever but in some cases there is a stage of secondary fever occurring from the 13th to 18th day The height of the temperature in this stage is less than that of the primary stage

ALIMENTARY SYSTEM The tongue is usually coated with a thick whitish fur Anorexia is present Abdominal pain and vomiting may in some cases be prominent feature The bowels are usually constipated though sometimes diarrhœa is met with The stools are pale in colour but may also be yellow

Liver The liver is usually enlarged 2 3 fingers breadth below the costal margin It is soft and tender

Gall bladder It may sometimes be palpable and tender

Spleen In most cases the spleen is not palpable

CIRCULATORY SYSTEM The pulse is at first soft and rapid in proportion to the temperature but with the appearance of jaundice it begins to slow down till a relative bradycardia occurs and persists even during the stage of secondary fever if there be any Pulse rate may be as low as 40 per minute with occasional extrasystoles on the 5th day of the disease Foetal and gallop rhythm may be present in severely toxic cases The blood pressure is often low

Hæmorrhages may occur into the skin or from various mucous membranes *in 50 per cent of cases* *There may* be petechiæ subconjunctival hæmorrhage bleeding from gums epistaxis hæmoptysis hæmatemesis melæna hæmaturia and menorrhagia

Blood examination shows slight or moderate hypochromic anæmia with a moderate or high leucocytosis The van den Bergh reaction is usually biphasic and the bilirubin content may be as high as 45 units Blood urea and non protein nitrogen are moderately high We have seen in one case the blood urea and non protein nitrogen to be as high as 410 mg and 245 mg per cent respectively

URINARY SYSTEM Usually on the 5th 7th day the urine is scanty bile stained and may show albumin red cells bile pigment hyaline and granular casts In severe cases hæmaturia is present Leptospiræ may be isolated from the urine after the first week

NERVOUS SYSTEM In some cases the onset is characterised by signs of meningeal involvement such as intense headache photophobia rigidity of the neck muscles and Kernig s sign

Atypical clinical types with or without jaundice are not infrequently encountered Following types have been described depending on the predominant presenting features

(*a*) *Tonsillar type*—Fever with sorethroat and generalised muscular pains may suggest a diagnosis of influenza or tonsillitis *Without manifest jaundice* these *cases may be missed* unless the true nature of the disease suspected from patient s occupation is confirmed by laboratory diagnosis

(*b*) *Abdominal type*—Fever abdominal pain vomiting with varying degrees of tenderness in the abdominal muscles may resemble an

acute abdominal condition A neutrophilic leucocytosis with hæmatemesis may lead to an erroneous diagnosis of perforated gastric ulcer

(*c*) *Respiratory type*—There may be physical signs of consolidation with hæmoptysis

(*d*) *Meningeal type*—Signs and symptoms of meningeal involvement may mask the true nature of the disease

(*e*) *Latent leptospirosis* without any jaundice and without any other signs and symptoms of illness may affect sewer workers Laboratory test alone can reveal this condition of asymptomatic leptospirosis

COMPLICATIONS

The following complications are met with in some cases

1 Uræmia 2 Acute circulatory failure 3 Bronchopneumonia 4 Severe hæmorrhages 5 Delirium convulsion and even paraplegia 6 Iritis and iridocyclitis

SEQUELÆ

1 Anæmia and asthenia—may persist for 2 3 months of convalescence 2 Pulmonary tuberculosis—due to reactivation of a latent tuberculous focus has been observed 3 Irregular pyrexia 4 Migraine like headache Liver and kidney functions are completely recovered

PROGNOSIS

The mortality varies from 5 30 per cent in different epidemics and in different countries It was about 33 per cent in the Calcutta cases In Japan it is about 50 per cent The prognosis is gloomy in presence of severe jaundice and hæmorrhages lung complications meningeal symptoms and uræmia The aged persons have a bad prognosis Death roll is heavier (33 per cent) in later age groups (over 60)

DIAGNOSIS

CLINICAL DATA 1 Sudden onset of high fever with severe headache pains in the joints and muscle especially those of the back and the leg 2 Pink conjunctivæ with or without jaundice 3 Presence of petechial spots 4 Fall of temperature with the appearance of jaundice 5 Presence of albumin red cell and cast in the urine

LABORATORY DATA. 1 Blood examination shows moderate or high leucocytosis

2 (*a*) Examination of the centrifuged deposit of fresh urine after the first week for *L icterohæmorrhagiæ* by dark ground illumination

(*b*) Culture of blood or other fluids (c s f) on Fletcher s medium for *L icterohæmorrhagiæ* within the first 5 days of the disease

(*c*) Animal inoculation (i) Intraperitoneal injection of 2 5 c.cm. of blood into guineapig before the 5th day of the disease and subsequent examination of the smears from blood the liver and spleen of the animal killed at the height of fever on the 4th day for presence of *L icterohæmorrhagiæ*

(ii) Inoculation of the guineapig with the centrifugalised deposit of urine taken under aseptic conditions from the patient after the 7th day may produce the disease

(*d*) Microscopical examination of tissue after staining

3 Serological—(*a*) Agglutination test of Schufiner—strongly positive after the 10th day A positive reaction may persist for months or even years after the attack Agglutination should be performed not only with local strains but also with the strains of different serological groups isolated in other parts of the world

(*b*) Brown (1939) has described an adhesion test Leptospira under the influence of homologous immune serum attract bacteria in colloidal suspension The patient s serum is mixed with a young culture of leptospira a living culture of some motile bacillus and fresh serum from guineapig the mixture is incubated at 37°C for half an hour Examined under dark ground illumination in a positive case motil bacilli will be found adhering to the leptospira

(*c*) Agglutination Lysis Test This test has been recognised as the method of choice in serological diagnosis (WHO)

DIFFERENTIAL DIAGNOSIS

INFLUENZA (*a*) Presence of upper respiratory tract catarrh (*b*) Early relative bradycardia (*c*) Leucopenia

MALIGNANT TERTIAN MALARIA (*a*) Frequent bilious vomiting and diarrhœa (*b*) Splenic enlargement (*c*) Presence of malaria parasites in blood

BLACKWATER FEVER Presence of hæmoglobinuria

DENGUE (*a*) Presence of an initial rash and also of the true measly eruption (*b*) Leucopenia

CEREBROSPINAL MENINGITIS (*a*) Presence of purulent spinal fluid showing marked increase of polymorphonuclear cells increase of

protein and diminution of sugar (*b*) *N. meningitidis* on smear and culture of the spinal fluid

After the appearance of jaundice when the temperature is near about normal leptospirosis may have to be differentiated from the following diseases by the following features

INFECTIVE HEPATITIS (*a*) Presence of marked anorexia nausea and vomiting (*b*) Slight rise of temperature (*c*) Hepatic enlargement often with tenderness (*d*) Often clay-coloured stool (*e*) Leucopenia

YELLOW FEVER (*a*) Comparative rarity of the disease (*b*) Presence of Faget's sign

RELAPSING FEVER (See under Relapsing Fever)

SECONDARY SYPHILIS (*a*) History of penile sore (*b*) Presence of characteristic roseolar rash with enlargement of lymph nodes (*c*) Positive Wassermann reaction and Kahn's test

GENERAL MANAGEMENT

It is the same as in any other infective fever

CONVALESCENCE Convalescence should be prolonged if necessary for 2-4 months or even more The patient should not be allowed to be up and about before the jaundice has cleared up and the heart sounds and the pulse rate are normal Anæmia requires prompt treatment with adequate doses of suitable iron preparations A daily movement of the bowels should be ensured by administration of one to two drachms of magnesium sulphate by mouth early in the morning Asthenia is to be treated with suitable tonics containing strychnine and vitamin B_1 Diet must not contain excess of fat and spice

SPECIFIC TREATMENT

High potency purified antiserum applied at an early stage gives excellent results Antibiotics to be of value must be started early by the 4th day of the disease Penicillin reduces the complication to a minimum Relatively high dosage 600,000 units of soluble penicillin at 6 hourly interval by intramuscular injection or aureomycin 0.5 g six hourly or oxytetracycline in the same dosage for 5 days is advised

SYMPTOMATIC TREATMENT

The objects of symptomatic treatment are (*a*) to maintain an efficient renal function by administration of alkalising diaphoretic and diuretic mixtures by intravenous injections of 0-100 c cm of 25 per

2 (*a*) Examination of the centrifuged deposit of fresh urine after the first week for *L. icterohæmorrhagiæ* by dark ground illumination

(*b*) Culture of blood or other fluids (c s f) on Fletcher's medium for *L. icterohæmorrhagiæ* within the first 5 days of the disease

(*c*) Animal inoculation (i) Intraperitoneal injection of 2 5 c cm of blood into guineapig before the 5th day of the disease and subsequent examination of the smears from blood the liver and spleen of the animal killed at the height of fever on the 4th day for presence of *L. icterohæmorrhagiæ*

(ii) Inoculation of the guineapig with the centrifugalised deposit of urine taken under aseptic conditions from the patient after the 7th day may produce the disease

(*d*) Microscopical examination of tissue after staining

3 Serological—(*a*) Agglutination test of Schuflner—strongly positive after the 10th day A positive reaction may persist for months or even years after the attack Agglutination should be performed not *only with local strains but also with the strains of different* serological groups isolated in other parts of the world

(*b*) Brown (1939) has described an adhesion test Leptospira under the influence of homologous immune serum attract bacteria in colloidal suspension The patient's serum is mixed with a young culture of leptospira a living culture of some motile bacillus and fresh serum from guineapig the mixture is incubated at 37°C for half an hour Examined under dark ground illumination in a positive case motile bacilli will be found adhering to the leptospira

(*c*) Agglutination Lysis Test This test has been recognised as the method of choice in serological diagnosis (W H O)

DIFFERENTIAL DIAGNOSIS

INFLUENZA (*a*) Presence of upper respiratory tract catarrh (*b*) Early relative bradycardia (*c*) Leucopenia

MALIGNANT TERTIAN MALARIA (*a*) Frequent bilious vomiting and diarrhœa (*b*) Splenic enlargement (*c*) Presence of malaria parasites in blood

BLACKWATER FEVER Presence of hæmoglobinuria

DENGUE (*a*) Presence of an initial rash and also of the true measly eruption (*b*) Leucopenia

CEREBROSPINAL MENINGITIS (*a*) P ulent fluid showing marked incre

CHAPTER II

RELAPSING FEVERS

[Spirochætosis Spirillum fever Febris recurrens]

DEFINITION

These are acute infectious fevers caused by certain Spirochætes transmitted to man through human lice or ticks and clinically characterised by alternate febrile and afebrile periods each of 5 to 10 days duration

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is known to occur epidemically or sporadically in the Continental Europe America Africa and Iran It is also prevalent throughout India except W Bengal Assam and part of Orissa

SEASONAL PREVALENCE It reaches its peak of incidence in March and April

AGE AND SEX INCIDENCE It is more common in adults than in children Males are more susceptible than females

PREDISPOSING FACTORS Poverty bad hygienic conditions over crowding starvation famine and war predispose to the disease by favouring louse infection

CAUSATIVE ORGANISM Relapsing fevers are caused by spirochætes of which there are several varieties morphologically similar but can be differentiated serologically The organism of the European type is *Spirochæta r currentis* discovered by Obermeier and formerly called after his name It is 10 to 30 *microns* long with numerous spirals actively motile gram negative and easily stained by Leishman s stain It is present in the blood in large numbers during the febrile period The causative organism of the Indian or Asiatic type of relapsing fever is *S cart ri* and that of the Central African type is *S duttoni*

MODE OF INFECTION

The European North American and Indian types of relapsing fever are conveyed by human lice (*P diculus humanus corporis*) Spirochætes appear in the blood of the lice after the 8th day and rapidly increase in number The irritation caused by the louse induces scratching and rupture of the louse during the process The released

cent glucose solution and by ensuring a fluid intake of 3 litres a day (*b*) to maintain an efficient circulation (*c*) to relieve distressing symptoms such as intense headache pains in the joints and muscle vomiting (*d*) to combat complications such as hæmorrhages by administration of 200 500 mg of ascorbic acid orally or intramuscularly Administration of vitamin K to raise the prothrombin content of the blood is often helpful

PREVENTIVE MEASURES

The preventive measures against leptospirosis consist of—

1 Destruction of rats of the infected areas 2 Protection of food and drink against contamination by the excreta of rats 3 Disinfection of the fæces and urine of the patients 4 Disinfection of the hands before taking meals 5 Protection of hands and feet of workers who are liable to get infected because of occupation 6 Avoidance of bathing and especially swimming with the crawl stroke in infected public baths pools and rivers 6 Prophylactic inoculation of persons who are liable to leptospiral infection by virtue of their occupation with a formolised or merthiolate vaccine

J C B

The relapse occurs on the 10th to 14th day and resembles the initial attack though the course is milder The number of relapses is one in most cases and two in some A third or fourth relapse is very rare In a few cases there may be no relapse and difficulties in diagnosis may arise

COMPLICATIONS

They are not common The following complications may be occasionally met with

1 Delirium convulsions meningitis 2 Iritis 3 Parotitis 4 Cervical lymphadenitis 5 Arthritis 6 Hæmorrhages into the skin and from the mucous membranes 7 Abortion in pregnant women

PROGNOSIS

The mortality varies from 2 30 per cent according to (*a*) the severity of the epidemic (*b*) constitution and age of the individual and (*c*) promptness of treatment Marked jaundice is of poor prognosis

DIAGNOSIS

Relapsing fever may be diagnosed from the following data

1 The character of the temperature chart 2 Presence of leucocytosis 3 Presence of spirochætes in the peripheral blood during the febrile period demonstrated by staining a thin film with Leishman s stain or by dark ground illumination 4 Presence of spirochætes in the blood of a mouse within 24 to 48 hours of its inoculation with 5 c cm of patient s blood 5 *Adhesion test*—Krantz has applied the Reichenberg reaction or adhesion test to relapsing fever spirochætes Specific immune serum causes the spirochætes and blood platelets to adhere together

DIFFERENTIAL DIAGNOSIS

MALARIA 1 Presence of malaria parasites in the blood 2 Prompt response to antimalarial drugs

INFLUENZA 1 Presence of a catarrh of the upper respiratory tract 2 Relative bradycardia 3 Presence of leucopenia

FILARIASIS 1 Presence of lymphadenitis and lymphangitis 2 Presence of microfilariæ in the blood

KALA AZAR 1 Insidious onset 2 Absence of gastro intestinal symptoms such as nausea vomiting and anorexia 3 Progressive leucopenia 4 Positive complement fixation antimony and aldehyde

spirochætes then enter any scratch or abrasion Lice remain infective for about one month

In the Central African type of relapsing fever the infection is conveyed by the contamination of the site of bite by the fæces and secretion of the coxal glands of the ticks Spirochætes are demonstrable in the salivary glands of ticks which also transmits the disease probably by biting The next generation of ticks is also infected through the ovum Both adult and larval ticks transmit the disease

PATHOLOGY

No specific pathological lesions are detectable Cloudy swelling and hyaline degeneration of various organs with an enlarged and congested liver and spleen may be present Congestive changes in the brain spinal cord and iris have been recorded specially with the *S duttoni* Microscopical examination may show spirochætes in the endothelial cells of the liver spleen and brain

LOUSE BORNE RELAPSING FEVER

[Epidemic relapsing fever]

CLINICAL MANIFESTATIONS

The incubation period is usually 5 to 7 days The *onset* is sudden with a rise of temperature up to 103° 104°F accompanied by headache rigor vomiting anorexia generalised pains The tongue is coated The bowels are either constipated or loose Spleen and liver are often enlarged and tender Jaundice may be present in majority of cases The lungs show signs of bronchitis in a large number of cases Blood examination reveals a polymorphonuclear leucocytosis with an increase of large mononuclear cells and also the presence of spirochætes during the febrile period A transient macular or petechial rash may occasionally be seen

Urine is frequently small in quantity and dark coloured showing the presence of albumin granular and hyaline casts and also spirochætes in the centrifugalised deposit Hæmaturia may occur

The temperature runs a continuous or remittent course coming down to normal by crisis on the 5th to 7th day with sweating followed by an afebrile period of the same length as the febrile phase Irregularities regarding the relative duration of the febrile and the afebrile periods are not uncommon but the sum total of the febrile and the afebrile periods is remarkably constant

Iran 2 It is transmitted to man by ticks infected from small rodents 3 The initial febrile period is short 2 3 days 4 Afebrile intervals vary from 1 21 days 5 The number of relapses is usually five to six sometimes as many as twelve 6 Relapses are as severe as the primary fever 7 Nervous complications such as optic atrophy cranial nerve palsies especially of the 7th nerve are not uncommon 8 Complications such as iritis diarrhoea and dysentery are more common 9 Scanty spirochaetes in the peripheral blood 10 Low mortality (about 5 per cent) 11 Larger doses of penicillin or arsenicals are necessary to control the disease Even then the arsenicals are never so useful as with louse borne variety Recently streptomycin in the dose of 0 5 g every 6 hours for 2 to 3 days or the broad spectrum antibiotic aureomycin in a dose of 2 g daily for a week has been used successfully

L K G

tests 5 Presence of flagellates on blood culture 6 L D bodies in marrow smears

HODGKIN'S DISEASE WITH PEL EBSTEIN SYNDROME. 1 Presence of enlarged firm and painless lymphatic glands on neck axillæ or groins 2 Presence of focal symptoms due to pressure of enlarged lymph nodes on neighbouring structures 3 Presence of eosinophilia in blood—occasionally 4 Biopsy of an enlarged superficial lymph node revealing the typical histological picture

DENGUE 1 Presence of relative bradycardia 2 Appearance of the characteristic rash 3 Presence of leucopenia

TYPHUS FEVER (See under Typhus Fever)

SPECIFIC TREATMENT

(1) ANTIBIOTICS *Penicillin* is the drug of choice When administered at 3 hourly intervals by intramuscular injection a total amount of 1 000 000 units a day for 7 days is usually needed

Aureomycin—It has a specific pronounced action Spirochætes often disappear after one dose 0 5 g administered 6 hourly for 2 days is effective

Streptomycin and other tetracyclines are also effective

(2) ARSENO BENZOL PREPARATIONS They are also specific for the disease Novarsenobillon in doses of 0 45 to 0 6 g dissolved in 10 c cm of freshly distilled water intravenously or sulpharsenol 54-60 centigrammes intramuscularly may be given to adults at weekly intervals The injections are usually given during the early febrile period to avoid collapse and not immediately before or during the crisis Usually 3 to 6 injections are required to control the disease Relapses may occur if less than 3 injections are given

GENERAL MANAGEMENT AND SYMPTOMATIC TREATMENT They are identical as in any other acute febrile diseases

PREVENTIVE MEASURES

The preventive measures are the same as in typhus fever

TICK BORNE RELAPSING FEVER

[Endemic relapsing fever]

The distinctive features from the louse borne type may be summarised as follows

1 It occurs sporadically in Central and North Africa Syria

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It varies from two to six weeks

MODE OF ONSET Fever comes on suddenly with headache rigor muscular aches anorexia vomiting and a rapid pulse In a few cases an epistaxis may herald the onset

The site of bite which had previously healed may now show evidences of inflammation There may be formation of a few vesicles and even ulcerations The lymph vessels draining the area may stand out as red streaks leading to the corresponding lymph nodes which are enlarged and tender Sometimes there may be a generalised lymphadenitis

The temperature rises to 103 104°F assumes a remittent character lasting for 3 to 6 days (Fig 32) and comes down by crisis with marked sweating Occasionally with the rise of temperature an urticarial maculopapular or less commonly a petechial rash may appear on the trunk limbs and face The rash may appear during each spell of fever or during the first spell only

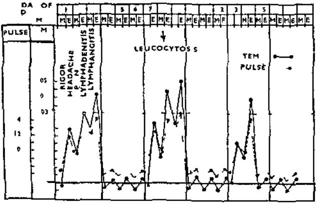


FIG 32 Typical temperature chart in rat bite fever with pyrexial waves

The crisis is followed by an afebrile period of 2 to 8 days when all symptoms disappear except weakness Then there is another bout of pyrexia for a few days to be succeeded by another afebrile interval The cycle of febrile and afebrile period lasting usually for 5 6 days thus repeats itself for weeks or months till the attacks are milder and a spontaneous cure ensues Blood examination shows anæmia and

CHAPTER III

RAT BITE FEVER

[Sodoku Cat bite disease]

DEFINITION

Rat bite fever is an acute infectious fever caused by *Spirillum minus* or *Streptobacillus moniliformis* transmitted to man through the bites chiefly of rats less commonly of cats dogs and other animal harbouring the parasite It is characterised clinically by a return of inflammation in the healed wound lymphangitis lymphadenitis fever with rigors and a purplish maculopapular rash

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is widely distributed throughout the world though it is very common in Japan In India it is not uncommon and in W Bengal it is rather more common than we are apt to think

AGE AND SEX INCIDENCE Adults are more frequently affected than children Both sexes are equally liable

CAUSATIVE ORGANISM There are two causative organisms The organism originally known as *Spirochæta morsus muris* now called *Spirillum minus* is one It is 2 to 5 *microns* in length with 2 to 3 regular curves actively motile and has flagella at both ends It is present in the blood during the febrile phase in the local lesion and also in the inflamed lymph glands The other is *Streptobacillus moniliformis* It may rarely cause rat bite fever in temperate climates The organism is straight or may be fusiform and is gram negative

MODE OF INFECTION

The *Spirillum* gains entrance to the human body through the bites or scratches of infected brown or black rats About 3 per cent of house rats are infected in Japan Occasionally moles cats dogs ferrets and other animals may convey the disease to man

PATHOLOGY

The local lesion is usually a non suppurative granuloma associated with perivascular roundcell infiltration Congestive and degenerative changes have been found in the liver kidneys and spleen

DIFFERENTIAL DIAGNOSIS

Rat bite fever has to be differentiated from the same diseases as considered under the differential diagnosis of relapsing fever

SPECIFIC TREATMENT

Penicillin is specific and may be used as in relapsing fever Other antibiotics as streptomycin and tetracyclines are also effective Arsenic was the standard treatment previously Usually two injections of neoarsphenamine in doses of 0 3 g and 0 4 g bring about a cure but 3 4 injections might be necessary in a few cases (*Banerjea*) Infections with *Streptobacillus moniliformis* usually do not respond to arsenic Antibiotics *e g* penicillin streptomycin however are useful in these cases

GENERAL MANAGEMENT AND SYMPTOMATIC TREATMENT They are the same as in any other febrile disease

PREVENTIVE MEASURES

PERSONAL PROPHYLAXIS Cauterisation of the site of bite with pure carbolic acid may prevent the entry of the spirillum into the blood

GENERAL PROPHYLAXIS Adoption of efficient measures for the destruction of rats They have already been described in the Chapter on Plague

L K G

leucocytosis with an increase of polymorphonuclear cells and eosinophils. The spirillum may occasionally be detected in the stained blood smear A positive Wassermann reaction may occasionally be present in cases of rat bite fever Kahn s flocculation test is more commonly positive

COMPLICATIONS

Usually there are no complications The following may rarely be present

1 Marked anæmia 2 Secondary pyogenic infection 3 Nephritis 4 Exophthalmos 5 Paresis 6 Photophobia and conjunctivitis 7 Endocarditis (specially with *Streptobacillus moniliformis*)

PROGNOSIS

The mortality is stated to be 10 per cent But probably with proper treatment it is as low as 1 per cent

DIAGNOSIS

The diagnosis is not difficult when the possibility of the disease is kept in mind in every case of protracted and relapsing fever The following data are helpful in the diagnosis

CLINICAL DATA 1 History of a bite by rat cat or dog 2 The characteristic temperature chart with pyrexial waves every th or 6th day 3 Presence of a local lesion associated with localised lymphangitis and lymphadenitis 4 Presence of rash

LABORATORY DATA 1 *Blood examination* It shows leucocytosis and occasionally the *Spirillum minus*

2 *Examination of the exudate* from the local lesions or the juice obtained by puncture of lymph glands may reveal the organism

3 *Animal inoculation test* During the febrile stage 5 c cm of blood are withdrawn and injected intraperitoneally into 5 white mice the blood and peritoneal fluid of which will show the spirilla from the 6th day onwards

4 *Immobilisation test with patient s serum* A guineapig previously infected with spirochætes is required for this test Diluted patient s serum is mixed with an equal volume of blood of infected animal on a slide Examination of the mixture after one hour shows immobile organisms A control test set up with normal saline shows actively motile spirilla A positive test definitely indicates rat bite fever but a negative result does not exclude this diagnosis

growth Best stained with Giemsa they usually present a more or less pleomorphic appearance Man is only casually involved The organisms are transmitted to man by some arthropod vectors like lice fleas ticks and mites Rodents like rat vole squirrel and bandicoot are important reservoirs of infection

They are mainly found within the mesothelial cells either in the nucleus or in the cytoplasm The serum of patient develops agglutinins for the proteus group of bacteria Rickettsia can only be cultivated in the yolk sac of growing chick embryo or in tissue culture Inspite of the small size and close relation to cells like viruses it more closely resembles bacteria under the electron miscroscope

A number of typhus like fevers has been described in different parts of the world The different groups may be classified on a geographical basis in terms of their insect vectors or according to their agglutination reaction with different strains of bacillus proteus

CLASSIFICATION

The typhus fevers may be classified according to the vector responsible for the transmission of the disease (*M gaa*)

1 Epidemic typhus fever
   Louse borne typhus
2 Endemic or epizootic typhus fevers
   (*a*) Flea borne typhus
   (*b*) Tick borne typhus
   (*c*) Mite borne typhus

EPIDEMIC TYPHUS FEVER

LOUSE BORNE TYPHUS

[European typhus Typhus exa thematicu Jail fever Camp fe er]

DEFINITION

It is an acute infectious epidemic disease caused by an intra cellular parasite *Rickettsia prowa eki* transmitted from man to man through infected lice and clinically characterised by sudden onset a remittent type of temperature with marked headache and stupor maculo papular rash and crisis on the tenth to the fifteenth day

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease occurs frequently as an endemic It is also prevalent in America Mexico Peru Manchuria

SECTION V DISEASES CAUSED BY RICKETTSIÆ

TYPHUS FEVERS

DEFINITION

Typhus fevers comprise a group of fevers caused by Rickettsia bodies clinically characterised by sudden onset of high remittent temperature associated with marked headache stupor typical rash and crisis on the tenth to the fifteenth day

HISTORY

Gerhard (1837) and Stille (1838) first distinguished typhus from typhoid fever Ricketts (1906) and Ricketts and Wilder (1910) transmitted Rocky Mountain spotted fever to guinea pigs through the bite of ticks and isolated Rickettsia bodies in the gut of infected lice

da Rocha Lima (1916) first brought out clearcut description of the Rickettsia bodies and named the causative organism of epidemic typhus as *Rickettsia prowazeki* Wolbach (1919) gave the name *Dermacentroxenus ricketts* to the causative organism of Rocky Mountain spotted fever Tsutsugamushi disease had long been known clinically as a disease transmitted by mite but it was only in 1923 that Sellards isolated the causative organism and designated it as *Rickettsia orientalis* Burnet and Freeman (1937) showed that Australian Q fever was caused by a rickettsia

Wilson (1909) first isolated from the stools of typhus patients proteus like organisms agglutinable by the patients sera Weil and Felix (1916) elaborated the specific agglutination test known by their names

Megaw (1917) pointed out the incidence of endemic typhus in India and suggested that the disease was probably transmitted by a tick The common typhus fever now occurring in India is caused by *Rickettsia orientalis* and transmitted through the arthropod vector *Trombicula deliensis* Recently a few cases of murine typhus have also been reported in India

GENERAL CHARACTERS OF RICKETTSIA

These minute bodies originally described by Ricketts are now known as *Rickettsia bodies* or *Rickettsiæ* They are non motile gram negative bodies with a diameter of 0 3 to 0 5 *micron* It is doubtful whether they are filterable Like viruses they require living cell for

lymph nodes present no definite abnormality Voluntary muscles show evidences of Zenker's degeneration as in typhoid fever *Rickettsia prowazeki* may be found in the typhus nodules

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually 8 to 14 days

STAGE OF INVASION Prodromata such as lassitude headache slight fever may be present for a day or two in some cases Onset is however usually sudden with a rapid rise of temperature chill rigor severe headache vomiting generalised pains flushing of the face and marked prostration The temperatre reaches its height (104° 106°F) on the third day (Fig 33) when the patient may be restless delirious or comatose The tongue is coated with a brownish white fur and may be tremulous The pulse is soft rapid in proportion to the temperature

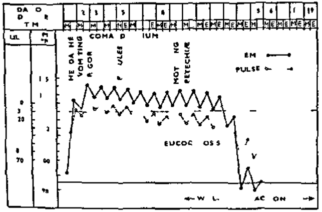


FIG 33 Temperature chart in a typical case of louse-borne typhus

STAGE OF ERUPTION The rash appears on the fourth to sixth day in the axillæ chest abdomen back and limbs Face neck palms and soles usually escape The rash consists at first of blotchy erythematous patches causing *subcuticular mottlings* and later of dull pink macules which assume on the sixth to eighth day a deep pink colour and in severe cases a petechial character resembling flea bites The macules are 2 6 mm in diameter By the tenth day the rash becomes deep brown and by the twelfth to fourteenth day it begins to disappear leaving a brown stain In mild cases however the rash may not show these changes At this stage headache increase and dry cough appears

and Northern Africa. It is a disease of cold and temperate climates. It is less common in the tropics. In hot climate the factors preventing the spread of the disease are scantiness of attire, custom of having regular daily baths and the lethal effect of tropical sun on lice.

SEASONAL PREVALENCE. It is most prevalent in December to April.

AGE, SEX AND RACE INCIDENCE. No age is immune. The disease is however mild in children. Both sexes are equally susceptible. All races are equally liable.

PREDISPOSING FACTORS. Bad hygienic conditions and overcrowding especially in the cold countries leading to louse infestation of the people, starvation, war and famine favour the outbreak and spread of the disease.

CAUSATIVE ORGANISM. The disease is caused by *Rickettsia prowazeki*, which is a gram negative, rod shaped, non motile organism 1 to 1.5 *microns* long and 0.3 to 0.4 *micron* broad. It is found in fæces of lice which had fed on the blood of typhus patient.

MODE OF INFECTION

The disease is usually conveyed to man by body lice (*Pediculus humanus corporis*) or less frequently head lice (*Pediculus humanus capitis*) which have been infective 8 to 10 days after feeding on the blood of typhus patients during the incubation and pre eruptive period. The organism gains access to the blood stream through the bitten area or an abraded area of the skin which becomes contaminated by the infective fæcal material of the louse. In the non epidemic period *human carriers* may play a role in spreading the infection. The Mexican and Manchurian types of epidemic typhus are transmitted also by rat fleas.

PATHOLOGY

Naked eye examination reveals no characteristic changes. The skin shows the petechial rash even after death. The spleen is congested, enlarged and soft. Liver and kidneys show signs of congestion.

Microscopic examination shows the characterised vascular lesions. These are called *typhus nodules*. They are situated in the walls of the capillaries and arterioles of the skin (corium), muscles, brain, kidneys and other viscera. These nodules are made up of focal multiplication of rickettsiæ, accumulations of mononuclear cells and degenerated endothelial cells. Hæmorrhages into the perivascular and the mesenteric

cartilages œdema of the glottis 2 Infarction abscess and gangrene of the lungs 3 Nephritis and cystitis 4 Hæmorrhages from the mucous membranes 5 Jaundice 6 Gangrene of the limbs due to arterial occlusion

SEQUELÆ

1 Femoral thrombosis 2 Cerebral vascular lesions *e g* thrombosis or embolism leading to paralytic phenomena 3 Mania melancholia and dementia—recovery occurs in a few month

PROGNOSIS

The average mortality before the introduction of pecific chemo therpy was about 10 to 20 per cent it is very low now The prognosis is grave under the following conditions

1 Age above 40 years 2 Marked toxemia associated with a high temperature restlessness sleeplessness delirium tremors of the tongue and fingers and coma vigil 3 Presence of circulatory failure 4 Hæmorrhages into the skin and from the mucous membranes 5 Lowered general resistance of the patient as a result of alcoholism dietetic deficiency 6 O currence of uræmic symptoms 7 Virulent epidemics

DIAGNOSIS

CLINICAL DATA 1 Sudden onset

2 Continuous fever associated with evere headache mental apathy and stupor and a soft rapid pulse from the b ginning

3 Appearance of rash on the 4th to 5th day

LABORATORY DATA 1 Presence of leucocytosis

2 Positive Weil Felix reaction in a titre of 1 in 160 or more even as much as 1 in 10 000 against *B proteus* OX19 from the 5th day onwards An agglutination test with rickettsia bodies has also been evolved

3 Animal inoculation Washed blood cells of patients injected intraperitoneally into guineapigs cause high fever and the animal usually dies within 2 weel At autopsy the animal shows characteristic nodes in the brain and rickettsia can be demonstrated in the lesions

4 Recently complement fixation test with specific rickettsial antigens has been found useful in the differentiation of different types of typhus fevers

5 Agglutination test with uspension of rickett iæ is more specific than the Weil Felix reaction

STAGE OF EXTREME PROSTRATION During this period the headache disappears as the toxæmia deepens and the nervous symptoms are aggravated Stupor and gradually coma supervene with tremor subsultus tendinum carphologia and coma vigil with involuntary passage of urine and stools In brief the patient passes into the typical typhoid state The abdomen shows no distension or tenderness The lungs may show signs of bronchopneumonia or hypostatic congestion The pulse is rapid and feeble The bloodpressure is very low Spleen is palpable in about 25 per cent of cases The blood shows a moderate leucocytosis 12 000 14 000 per c mm with an increase of polymorphonuclear cells The serum of typhus fever patients taken after the fifth day of the disease agglutinates *B proteus* OX19 in high titre (*Weil Felix reaction*) The Wassermann reaction is almost always positive in typhus when blood is examined during the acute stage but becomes negative again in convalescence In inoculated persons the titre of Widal reaction for typhoid fever rises (an *anamnestic reaction*) The urine frequently shows albumin due to larval nephrotic changes The cerebrospinal fluid may show slight lymphocytosis with increase of globulin content and weakly positive Weil Felix reaction In severe cases death occurs from cardiac failure In favourable cases crisis occurs on the tenth to the fourteenth day followed by disappearance of the rash in about a week leaving brownish stains in the skin In some cases the fever comes down by lysis The occurrence of relapses is rare Moreover an attack of louse borne typhus protects against flea borne typhus

CLINICAL TYPES

MILD TYPE It usually occurs in endemic areas especially in children

SEVERE TYPE (*Typhus siderans*) It may end fatally on the second or third day of the disease

MENINGEAL TYPE It is associated with signs and symptoms of meningeal irritation

HÆMORRHAGIC TYPE It is associated with hæmorrhage into the skin and from the mucous membranes

COMPLICATIONS

COMMON COMPLICATIONS 1 Bronchitis bronchopneumonia and hypostatic congestion of lungs 2 Cardiac and peripheral failure 3 Suppurative parotitis 4 Femoral thrombosis 5 Bedsores

RARE COMPLICATIONS 1 Laryngitis necrosis of the laryngeal

3 to 4 hours the response appears to be similar to that of chloram phenicol

3 *Oxyt tracycline* Successful treatment of various types of typhus fever with this antibiotic has also been reported

The general and symptomatic measures to be adopted in the management of typhus fever are identical with those described in the treatment of typhoid fever

In severe and late ca es combined use of corticosteroids and broad spectrum antibiotics give excellent result

PREVENTIVE MEASURES

1 Use of anti louse powder—Thi powder contains 10 per cent D D T and can be used even when a person is fully clothed by blowers Three applications of this powder at weekly interval eliminates nits and lice

Impregnated clothing with 1 per cent D D T is very effective anti lice measure

In addition shaving of the body including pubes and axillæ cropping of hairs of the scalp are also advocated

2 Disinfection of bed and clothing of the patients and their contacts by dry heat boiling or by oaking in 2 per cent lysol olution D D T is best for this purpose

3 Wearing of caps gowns and rubber gloves to protect against lice

4 Delousing and quarantine of contacts for 15 days

5 Prophylactic inoculation with a vaccine prepared by growing the *Rickettsia prowa eki* in lice (Weigl) or in the volksac of chick embryo has been u ed with some success

BRILL S DISEASE

It is a variety of lou e borne typhus endemic in character and not transmissible by lice to contacts It is probably a recrudescence of epidemic typhus in a subject who had the disease previously in a latent form The causal agent re embles *R prowa cki* In America the nomenclature of Brill s di ease is used for fever seen in immigrants from Europe only

ENDEMIC TYPHUS FEVERS

This group of fevers occurs primarily as an epizootic in the rodents such as rat ground squirrel rabbits etc and affects man secondarily through vectors such as fleas ticks and mites

DIFFERENTIAL DIAGNOSIS

In the tropics typhus fever is to be differentiated from the following diseases

TYPHOID FEVER 1 Continued pyrexia 2 Slow pulse in relation to the temperature 3 Presence of the signs and symptoms of the enteric group of fevers 4 Blood culture and Widal's test positive to *Bact paratyphosum*

CEREBROSPINAL MENINGITIS (*a*) Sudden onset (*b*) Persistent headache (*c*) Signs of meningeal irritation (*d*) Lateral decubitus with head retraction (*e*) Leucocytosis (*f*) Turbid or purulent spinal fluid showing increase of protein and polymorphonuclear cells disappearance of glucose and present of *N meningitidis* in the smear from centrifugalised deposit and on culture

SMALLPOX 1 Absence of well foveated scars of a successful vaccination 2 Severe constitutional disturbances 3 The occasional prodromal groin rash 4 Appearance of the maculopapular eruption on the 3rd to 4th day and the subsequent gradual evolution 5 The characteristic centrifugal distribution of the eruption

MEASLES 1 Presence of oculo na o pharyngeal catarrh 2 Appearance of Koplik's spots on the second day 3 The blotchy crescentic maculopapular rash appearing on the forehead along the hairy margins and behind ears

SCARLET FEVER 1 Presence of a persistent punctate erythematous rash 2 Presence of sore throat and the characteristic furred strawberry tongue

SPECIFIC TREATMENT

Clinical observation regarding the unfavourable influence of sulphonamides led to the use of para aminobenzoic acid (which competitively inhibits the action of sulphonamide) The drug was effective in a dose of 15 20 g daily but has now been superseded by the following antibiotics

1 *Chloramphenicol* is the drug of choice It is used in the dosage of 0 25 g every 4 hours and it specifically controls the disease within 2-4 days The dose may be doubled in very severe cases Chloramphenicol may also be given intramuscularly where necessary

2 *Aureomycin* This antibiotic has been very useful in the treatment of epidemic typhus A satisfactory result has also been reported in some of the other types Given in a dosage of 0 25 g every

TICK BORNE TYPHUS

[Rocky Mountain spotted fever Indian tick typhus]

VARIETIES

Many clinical varieties of tick borne typhus have been described according to the places of occurrence They are all similar in many aspects differing only in some points The characteristic type is Rocky Mountain spotted fever

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease was formerly considered to be prevalent only in the Rocky Mountains and the Pacific Coast States of America but its occurrence in the Central and other States of America is now recognised

SEASONAL PREVALENCE In the Rocky Mountains it is most prevalent in April and May whereas in the Eastern States it is chiefly seen in the autumn

CAUSATIVE ORGANISM The disease is caused by *R rickettsii* (*Dermacentroxenus rickettsi*) morphologically almost similar to *R prowazeki*

MODE OF INFECTION

The organism gains entrance to the human tissues through the bites of adult ticks (*Dermacentor andersoni*) which have become infected in the larval stage from the various infected rodents of the hills such as ground squirrels rabbits etc Dogs may sometimes carry infected ticks and spread the disease

PATHOLOGY

Same as that of louse borne typhus *R rickettsii* is found within the nucleus of mesothelial cells and not in the cytoplasm as with *R prowazeki*

CLINICAL MANIFESTATIONS

The incubation period is 2 14 days or may be longer The clinical picture is similar to that of louse borne typhus except on the following points

1 Fever is more often remittent ending by lysis in 2 3 weeks 2 Relative bradycardia often present 3 The macular or papular rash usually appears on the 3rd-4th day first on the wrists and ankle and then all over the body The palms soles scalp and face are not exempted 4 Hæmorrhagic complications are rather common such

FLEA BORNE TYPHUS

[Endemic typhus Murine typhus]

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It has a world wide distribution occurring chiefly in the Mediterranean areas South Africa the Malaya Peninsula the Dutch East Indies and Manchuria It is also prevalent to a certain extent in India (especially the Simla hills Bombay Calcutta) Australia South America and Russia

CAUSATIVE ORGANISM The disease is caused by *Rickettsia typhi* (*R mooseri R murina*) which is closely related to *R prowazeki*

MODE OF INFECTION

The organism is conveyed to man by the rat flea *Xenopsylla cheopis* from infected wild rats

PATHOLOGY

The pathological changes in infected animals are the same as in louse borne typhus except in the guinea pig which shows the Neill Mooser reaction characterised by swollen testicle with greatly inflamed tunica showing exudate and hæmorrhage No postmortem studies on human material are available

CLINICAL MANIFESTATIONS

The clinical picture resembles that of a mild louse borne typhus The eruptions are often scanty and may be absent An attack of flea borne typhus protects against louse borne typhus but not against the other forms of typhus fevers

PROGNOSIS

The mortality is extremely low

DIAGNOSIS

It is based on the following data 1 Absence of epidemics 2 Absence of a local sore with enlargement of regional lymph nodes 3 Rash scanty or absent 4 Positive Weil Felix reaction against Proteus OX19 and negative or occasionally positive reaction against Proteus OXK 5 Positive rickettsia agglutination and complement fixation tests 6 Inoculation tests with blood in rats and guineapigs positive In the guineapig characteristic Neill Mooser reaction (inflammation of the tests) is seen

TREATMENT

Broad spectrum antibiotics are effective

OX19 and slightly positive to OXK and OX2 8 Average mortality is about 5 per cent

MITE BORNE TYPHUS

[Scrub typhus Tropical typhus Japanese river fever Tsutsugamushi disease Indian XK typhus Delhi pseudo typhus]

The classical form of mite-borne typhus is the Japanese river fever

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is chiefly prevalent in the riverine areas of Japan but it also occurs in Formosa China Sumatra Malaya Vietnam the Philippines and Northern Queensland The disease occurs also in India and Burma Recently the disease has emerged from comparative obscurity to notoriety

SEASONAL PREVALENCE In the tropical countries the disease may occur at any time of the year though in Japan the highest incidence is between June to October

AGE AND SEX INCIDENCE It is liable to occur at all ages There is no special predilection for any particular sex

OCCUPATION Workers who handle grains gather hemp or labourers who are engaged in the palm plantations in clearing and pruning palm trees are especially liable to the disease

CAUSATIVE ORGANISM The disease is caused by *Rickettsia tsutsugamushi* (*R orientalis*) which is conveyed to man by the larva of a red mite of the genus *Trombicula* which has previously been infected in the adult stage by biting infected rats or mice and transmitted the virus to the offspring In Japan the disease is transmitted by *T akamushi* in India by *T deliensis* and in New Guinea by *T fletcheri*

CLINICAL MANIFESTATIONS

Incubation period is 5 14 days The mode of onset and the temperature are same as in Rocky Mountain fever The following are however the special features of this disease

1 Appearance of a local eschar lymphadenitis and lymphangitis 3 4 days after the bite though not invariable 2 Rash is maculo papular and affects usually the face and trunks but less frequently the palms and soles 3 Leucocyte count is variable and there may be neutropenia During the first nine days the count tends to be of low normal type i e 4 000 to 6 000 cells per c mm but later on the

as epistaxis hæmaturia and melæna 5 Moderate leucocytosis 6 It does not protect against other forms of typhus fever

LABORATORY DATA 1 Weil Felix reaction is positive against *B proteus* OX19 in a titre over 1 in 300 Sometimes this reaction is more strongly positive against *B proteus* OXK or OX2 than against OX19 2 Rickettsiæ agglutination plus complement fixation test 3 Occurrence of a marked scrotal swelling with necrotic changes in guineapigs after inoculation with the blood of the patients in severe cases of tick borne typhus

DIFFERENTIAL DIAGNOSIS AND TREATMENT

Same as those of louse borne typhus

PREVENTIVE MEASURES

It consists of the following measures

1 Avoidance of infected areas and wearing of tick proof clothing 2 Prompt removal of the ticks from the body 3 Local application of liquor iodine to the bitten area or excision of the same if the tick is firmly adherent to it 4 Prophylactic inoculation with a vaccine made from the rickettsiæ killed by formalin and from the carbolised emulsified tissues of artificially infected ticks It confers a high degree of immunity 5 Use of gammexane against ticks

INDIAN TICK-BORNE TYPHUS

This was described by Megaw in 1917 Later Heilig and Naidu (1942) reported similar cases from Mysore

The characteristic features may be summarised as follows

1 It occurs in India especially in the Himalayan region South Western parts of the Punjab and the Uttar Pradesh 2 It is usually a non epidemic tick borne disease transmitted to man by a tick (probably *Rhipicephalus sanguineus* or *Hyalomma ægypticum*) which has become previously infected by biting squirrels or rabbits in the hills or forests 3 History of a tick bite or a cutaneous wound with enlarged glands due to the bite may be present in a few cases In many cases the tick may be found attached to the site of the bite 4 The rash usually appears on the 3rd to 5th day and does not spare the face or the palms and sole The scalp however escapes 5 Splenic enlargement is rare 6 Jaundice and alubuminuria are absent 7 Weil Felix reaction is either strongly positive to *B proteus* OX2 and slightly positive to OX19 and OXK or moderately positive to

population due to partial immunity but as high as 40 per cent in the newcomers such as Europeans

3 TROPICAL SCRUB OR RURAL TYPHUS It is characterised by the following features (a) It affects especially the troops fighting in infested jungle areas and the labourers in palm plantations and coming in contact with dead palm flowers (b) The causative organism *is the same as in Japanese river fever (Leuthwaite and Savoor)* (c) The causative organism is transmitted by *T delicnsis* from the infected rats (d) Rash is often faint or even absent (e) Mortality is 10-14 per cent (f) Complete control of scrub typhus may be brought about by a fortnightly rubbing of an ounce of D B P (dibutyl phthalate) into the socks trousers shirts and underwears

4 THE COASTAL FEVER OF QUEENSLAND (*Mossman Fever*) The main characteristics are (a) The incidence of the disease is chiefly amongst sugarcane workers (b) It is a mild type of mite borne typhus (c) A local sore is absent though lymphadenitis and lymphangitis may be present (d) Mortality is about 1 per cent

OTHER RICKETTSIAL FEVERS

The other Rickettsial fevers are Trench fever Q fever and Rickettsial pox

A comparative study of the essential features of the common Rickettsial diseases is shown in a tabular form

J C B

leucocyte count almost always returns to average normal level In fatal cases there may be marked leucopenia all along 4 Pulmonary complications are common with signs and symptoms suggestive of bronchitis or bronchopneumonia 5 Nervous system—Mental symptoms are always seen in the seriously ill patient An initial feeling of apathy with occasional euphoria may lead to restless irritability toxic confusion and wild delirium Other patients become apathetic drowsy and stuporous Neurological complications include tremor photophobia tinnitus nerve deafness neuritis and urinary incontinence or retention There may be signs and symptoms of increased intracranial pressure al o 6 A strongly positive agglutination response to *B proteus* OXK and negative or weak response to OX19 or OX2 7 Inoculation of white mouse with washed blood cells of the patient produces a fatal illness with ascites and splenomegaly Rickettsiæ in large numbers can be demonstrated in the peritoneal exudate 8 The mortality varies from 20 40 per cent 9 It confers no immunity against the other forms of typhus fevers

TREATMENT

Same as in louse borne typhus

PREVENTIVE MEASURES

The preventive measures consist of

1 Avoidance of endemic areas 2 Use of mite proof clothing 3 Burning down of the bushes in the endemic areas 4 Sterilisation of clothing used in the infected fields 5 While working in the mite infested country anti mite fluids such as dibutyl phthalate should be sprinkled over the wearing apparels beddings and other articles liable to be infested with mite 6 The status of an effective vaccine prophylaxis is still in the experimental stage

OTHER CLINICAL VARIETIES OF MITE TYPHUS

1 INDIAN MITE BORNE TYPHUS It is characterised by (*a*) Endemicity in certain areas (*b*) Incidence in August to September (*c*) Rare presence of the local sore Lymphadenitis may however be present (*d*) Agglutination test strongly positive to *B proteus* OXK and negative to OX19 or OX2

2 PSEUDO TYPHOID FEVER OF SUMATRA It is characterised by the following features (*a*) The causative organism is transmitted by *Trombicula deliensis* from infected rats (*b*) Local sore is usually absent (*c*) Mortality is as low as 5 per cent in the indigenou

TABLE SHOWING A COMPARATIVE STUDY OF THE ESSENTIAL FEATURES OF THE RICKETTSIAL DISEASES

Disease and its synonyms	Geographical distribution	Causative organism	Insect vectors	Reservoir	Serum agglutination response			Rash	Mortality (Per cent)
					OX19	OX2	OXK		
Trench fever Five day fever	Poland N. Africa	*R. quintana*	Louse (*P. humanus*)	Man	—	—	—	Red macules lasting for 6-48 hr usually seen in first febrile bout tendency to relapse	0 to 1
Q fever	Australia Europe U.S.A.	*Coxiella burnetii*	Tick (*D. andersoni*)	Bandicoot	—	—	—	Nil	0 to 3
Rickettsial pox	New York City	*R. akari*	Mite	Mice	—	—	—	Maculo papular on 1st to 4th day of fever	Nil

TABLE SHOWING A COMPARATIVE STUDY OF THE ESSENTIAL FEATURES OF THE RICKETTSIAL DISEASES

Disease and its synonyms	Geographical distribution	Causative organism	Insect vectors	Reservoirs	Serum agglutination response			Rash	Mortality (Per cent)
					OX19	OX2	OXK		
LOUSE BORNE TYPHUS Epidemic typhus Typhus exanthematicus	Cosmopolitan Less common in the tropics	*R. prowazeki*	Louse (*Pediculus humanus*)	Man	++++	− or +	−	Macular or papular often faint Face sole palms usually free	10 to 20 May be more
FLEA BORNE TYPHUS Endemic typhus Murine typhus	World wide	*R. typhi*	Rat flea (*Xenopsylla cheopis*)	Rats Mice	++++	− or +	−	Macular or papular often faint or absent	10 or less
TICK BORNE TYPHUS Rocky Mountain spotted fever	Rocky Mountain States U. S. A.	*R. rickettsii*	Tick (*Dermacentor andersoni*)	Goats Hares Rodents	++++ or +	+ or ++++	−	Maculo papular Common on face soles palms	10 to 80
MITE BORNE TYPHUS Scrub typhus Tsutsugamushi disease Tropical typhus	Japan Formosa Malaya Java Sumatra New Guinea India	*R. tsutsugamushi*	Larva of mite of the genus Trombicula In India the vector is *Trombicula deliensis*	Vole Rat Bandicoot	−	−	++++	Macular or papular often on face Rare on palms and soles	10 to 30

Causative Organism Smallpox is caused by a filterable virus the diameter of which varies from 250 to 400 *millimicrons* It is present in large numbers in the exudate of the vesicular and pustular lesions of smallpox A pure suspension of the virus obtained from the variolous lesions is agglutinated by the sera of patients convalescent from small pox The virus is easily killed by antiseptics but highly resistant to desiccation

Certain minute cell inclusions called *Guarnieri bodies* are found in the disintegrated epithelial cells of the vesicular lesions of smallpox and vaccinia They were at one time thought to be harbouring a protozoal organism (*Cytorrhyctes variolæ*) Paschen has however shown that some of these Guarnieri bodies contain the *Elementary bodies* though others may represent degenerative reactions of the tissue cells to the infection

MODE OF INFECTION

The virus gain entrance to the body through the mucous membranes of the nose mouth upper respiratory tract in one of the following ways

1 Contact Infection Contact with the patient in the infective stage which begins even before the appearance of the rash reaches its height during the eruption and ends with the complete decrustation is the usual mode of infection Contact with infected clothes and articles used by the patient is also responsible for transmitting the disease to healthy persons

2 Human Carriers or Intermediaries Healthy persons may carry the germ in their clothes hair and thus infect other persons

3 Aerogenous Infection At one time it was held that the virus in the dry scales was transmitted to long distances as much as a mile through the medium of air But this view is no longer accepted by most authorities

4 Inoculation Such a mode of infection is possible but most improbable

PATHOLOGY

The pathological lesions of smallpox consist essentially of (*a*) lesions of the skin and mucous membranes (*b*) visceral changes and (*c*) blood changes

Cutaneous Lesions The prickle cells of the deeper layers of the skin undergo a colliquative necrosis with softening and accumulation of serous fluid inside and between the cell bodies resulting in the

SECTION VI DISEASES CAUSED BY VIRUSES

CHAPTER I

SMALLPOX

(Variola)

DEFINITION

It is an acute specific infectious disease caused by a filterable virus (*Elementary bodies of Paschen*) and clinically characterised by high fever associated with severe headache backache and a characteristic eruption which passes successively through the stages of macule papule vesicles pustules and crusts

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION Smallpox has a world wide distribution though it is chiefly a disease of the tropical countries such as India Africa and China where it is endemic Outbreaks of smallpox especially of the mild type are not uncommon in western countries as France England and America The disease occurs in an epidemic form in W Bengal

SEASONAL PREVALENCE In thé tropical countries smallpox reaches its peak of incidence in February showing a decline in the rainy reason due to high absolute humidity In cold countries the disease occurs chiefly in the late winter and early spring

AGE AND SEX INCIDENCE Persons of all ages are attacked by the disease unless they are protected by a previous attack or by a successful vaccination The infants and children of an unvaccinated community are often attacked The fœtus in the uterus may contract infection if the mother suffers from it during pregnancy The child if it survives may be born with the rash or the scars There is another group of cases where the child develops the rash within 14 days of birth the infection occurring in the uterus or during separation from the mother who was in the pre eruptive or early eruptive stage at the time of delivery If the child is born however in the eruptive stage of the mother it develops rash earlier Both sexes are equally liable to the disease

RACE The coloured races are said to be especially susceptible because they remain unvaccinated either through superstition or negligence

sudden characterised by chill and rigor severe headache rapid rise of temperature to 104 105°F which continues with slight remission for 3 4 days (Fig 34) and is associated with soft rapid pulse hurried breathing prostration severe pain in the loins back and the limbs and vomiting In addition marked flu hing of the face with congested eyes restle sness insomnia and delirium may be present Splenic enlargement is frequent In children convulsions and vomiting are often present

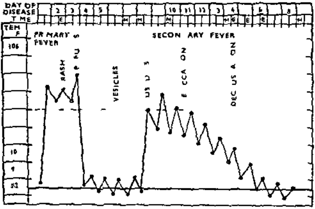


FIG. 34 Temperature chart in a typical case of smallpox

A transient prodromal rash may occasionally be een at this stage in 10 15 per cent of smallpox patients with a fair and white skin This rash may be either erythematous (measly urticarial or scarlatinal) or less frequently petechial The erythematous type appears on the second day of the disease on trunk limbs and rarely the face The petechial type is distributed over the lower abdomen groins axillæ popliteal fossa and back of neck and may last till the appearance of the maculo papular eruptions

Erupti e period Red *macules* 2 3 mm in diameter slightly fading on pressure appear on the 3rd to 4th day first on the forehead wrists and hands Then the trunk and low r extremities are involved The eruption of macules is compl te within 24 hours The macules *soon* change to *papules* which are solid elevations in the skin with a shotty feel The distribution of the eruptions is characteristically centrifugal They are mo t numerous on the upper part of the face wrists hand feet and upper part of the back They are scanty over the chest

formation of a vesicle which is multilocular due to the persistence of strands of degenerated epithelial cells The umbilication of the vesicle occurs as it distends peripherally the centre being bound down by the trabeculæ When suppuration occurs the reticular strands are destroyed and lesion becomes unilocular and dome shaped

LESIONS IN MUCOUS MEMBRANES The mucous membranes of the nose mouth tongue palate pharynx and larynx and even occasionally of the bronchi œsophagus and stomach may show vesicles which being constantly bathed in secretions quickly ulcerate Vesicular and ulcerative lesions may also be seen in the mucous membranes of the conjunctiva vulva vagina and the rectum

HÆMORRHAGES In severe cases hæmorrhages may occur on the second to fourth day of the disease in the skin and from mucous membranes of the gastrointestinal respiratory and urinary tracts The characteristic papulovesicular eruption may be ab ent In other cases hæmorrhages may occur into the vesicles and pustules

VISCERAL CHANGES At autopsy liver spleen and lymph glands are enlarged The heart liver and kidneys may show cloudy swelling and fatty infiltration The lungs may show bronchopneumonic changes The liver testicles and bone marrow may show areas of necrosis as ociated with mononuclear cell infiltrations In the hæmorrhagic types of smallpox hæmorrhages may be present in the serous sacs lungs and retroperitoneal tissues

BLOOD CHANGES There is marked involvement of the blood vessels and the reticuloendothelial system in particular giving rise to the hæmorrhagic tendency The blood shows a leucocytosis of 15 000 to 20 000 per c mm with marked increase of the mononuclear cells and decrease of the polymorphs increase of the eosinophils and presence of myelocytes 3 5 per cent or even more in the invasive stage of the disease In the stage of pustulation a leucocytosis of 20 000 to 40 000 per c mm with an increase in the polymorphs occurs A moderate anæmia is often present A diminution in the platelet count may be present especially in the hæmorrhagic types of the disease Bleeding time is raised and coagulation time remains within normal limits in the e cases

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually 12 days from the exposure though it may vary from 10 15 days

MODE OF ONSET *In asive period* The onset of the disease is

temperature and constitutional symptoms may not occur with the appearance of the eruptions There is severe toxæmia in this group associated with high continued secondary fever rapid pulse and delirium due to presence of marked inflammatory swelling and the formation of large subcutaneous abscesses which give rise to an extreme fetor Severe conjunctiviti soreness of the mouth dysphagia hoarseness or loss of voice and difficulty in breathing are often present Death usually occurs from circulatory failure on the tenth to twelfth day

HÆMORRHAGIC FORM Generally it occurs amongst the unvacci nated persons Two types of the disease are met with

1 *Purpura variolosa (Petechial smallpox or Black smallpox)* The disease starts with severe prodromal symptoms and the toxæmia is severe Hæmorrhages under the skin and from the mucous membranes appear on the first to third day of the illness in the pre eruptive period The cutaneous hæmorrhages which are petechial in mild cases but ecchymotic in severe cases are usually found over the lower abdomen and upper parts of the thighs (the bathing drawers area) Subconjunctival hæmorrhages are often present Hæmorrhages from the various mucous membranes may give rise to hæmatemesis melæna hæmoptysi hæmaturia and even metrorrhagia Of these hæmaturia is probably most common Hæmorrhages may also occur into the various serous sacs such as pleuræ peritoneum The fever does not show the usual remission on the fourth day but continues till the fifth to the eighth day when the papules appear In severe cases the temperature is subnormal due to associated collapse and the patient may die before the appearance of any eruption In course of this disease the mind remains clear upto the end Respirations are rapid and shallow the pulse rate is unduly rapid 140 160 per minute The liver is often enlarged and the spleen may in some cases be palpable The blood examination shows marked leucocytosis with an increase of mononuclear cells A few myelocytes may be present

2 *Variola pustulosa hæmorrhagica* The di ease which is more common than purpura variolosa has a very severe onset and hæmorrhages may occur around and into the papules vesicles or pu tules Bleeding from the mucous membranes may also be present It usually proves fatal on the eighth or ninth day

MODIFIED FORM (*Varioloid*) It occurs in vaccinated persons and is often mi taken for chickenpox It commences as an ordinary

abdomen and legs and usually *absent in the lower two quadrants of the abdomen* (*Gasparini's sign*)

Smallpox rashes always appear in a definite order Rashes first appear on the buccal and pharyngeal mucosa *often giving rise to sore throat* hoarseness and cough Next they appear as cutaneous lesions first on the forehead and in some cases on the wrists and then spread on to the face arms trunk and lastly on the legs

Eruptions may appear in the palpebral conjunctivæ external auditory meatus urethral meatus vulva vagina and the anus

With the appearance of the maculo-papular eruption the temperature drops down to normal or near about that level the general symptoms subside and the patient passes into a comfortable state On *the fifth to sixth day* the papules change into *pearly vesicles* due to collection of fluid Each one of them is firm elevated circular and multilocular It presents a little depression in the centre (*umbilication*) and is surrounded by a small red areola On the *eighth to ninth day the fluid* becomes turbid and purulent turning the vesicles into pustules which are dome shaped and the umbilication is lost This maturation first takes place on the face and follows the order of appearance of the eruptions With the formation of pustules due to a secondary pyogenic infection the temperature rises with a return of the constitutional symptoms (*secondary or suppurative fever*) Swelling of the face and eyelids thirst dysphagia and delirium may be present The pustules begin to dry up (*stage of desiccation*) by the *eleventh to twelfth day* forming yellow *crusts* first on the face and then on the other parts The fever also comes down gradually with the drying of the pustules By the *fourteenth* or *fifteenth day* the process of separation of crusts (*decrustation*) is fairly advanced though it may take three or four weeks to be completed especially in the palms and soles where the very thick skin prevents the rupturing of the pustule

The character of the eruption varies widely in different epidemic and according to the variations the following clinical types may be described

CLINICAL TYPES

DISCRETE FORM This form in which the cutaneous lesions remain separate from one another has been described above

CONFLUENT FORM In this form the eruptive lesions especially over the face hands and feet coalesce either in the papular stage or more commonly in the pustular stage The usual remission of the

COMPLICATIONS

Complications are particularly frequent in the confluent type of small pox though they may occur in the other forms of the disease

RESPIRATORY SYSTEM 1 Laryngitis which may lead to œdema of the glottis perichondritis and necrosis of the laryngeal cartilages 2 Pneumonia and bronchopneumonia occurring in about 40 per cent of fatal cases 3 Pleurisy serofibrinous or less frequently purulent 4 Lung abscess

CARDIOVASCULAR SYSTEM 1 Acute circulatory failure common in the severely toxic cases 2 Hæmorrhages due to toxic action on the blood vessels 3 Pericarditis and endocarditis rare 4 Myocarditis not uncommon

DIGESTIVE SYSTEM 1 Hæmorrhages from the stomach and intestines 2 Diarrhœa 3 Parotitis 4 Retropharyngeal abscess rare

URINARY SYSTEM 1 Albuminuria with or without casts due to a toxic nephrosis common 2 Nephritis and uræmia rarely

GENITAL SYSTEM 1 Premature onset of menstruation during the invasion stage 2 Epididymo orchitis (*Chiari*) 3 Gangrene of vulva penis and scortum rarely

NERVOUS SYSTEM 1 Convulsion in children in the prodromal stage 2 Delirium and coma 3 Acute disseminated encephalo myelitis and spinal myelitis 4 Peripheral neuritis 5 Psychoses

EYES The complications are either due to the actual eruptive lesions or to secondary pyogenic infection 1 Purulent conjunctivitis a common complication 2 Corneal ulcer 3 Diffuse keratitis 4 Blepharitis 5 Iridocyclitis and retinal hæmorrhages rare

EAR Otitis media

SKIN 1 Multiple boils 2 Large superficial cutaneous abscesses where the whole epidermis may peel off seen in confluent type of cases 3 Cellulitis erysipelas and septicæmia may result from pustules and abscesses 4 Bed sores and gangrene of the skin in severe cases

BONES AND JOINTS 1 Osteomyelitis may occur due to a secondary pyogenic infection or due to the virus of the smallpox itself (*osteomyelitis variolosa*) 2 Arthritis occasionally seen suppuration in children due to a secondary streptococcal infection

PREGNANCY Abortion or premature delivery is very frequent occurring in about 60 per cent and it may be followed by septicæmia

smallpox though milder in its initial symptoms The following features are noticed

1 *Eruptions* They are scanty and may appear at the usual time or with the onset of the fever

2 *Fever* Either there is no fever or if present it may last for one to three days only The secondary fever is absent

3 *Character of the eruptions* The pustular stage may not be reached Desiccation may begin in the papular or vesicular stage The characteristic centrifugal distribution is however maintained If pustules form at all they disappear within twenty four hours

ABORTIVE FORM It occurs both in the vaccinated and unvaccinated people The initial symptoms of headache backache fever and vomiting may be present but the clinical course is very mild Eruptions are very scanty and the disease is over in a few days Sometimes the vesicles begin to dry up without passing through the pustular stage Rarely small pox may abort completely the characteristic eruptions not appearing at all (*variola sine variolæ*)

MILD FORM (*Variola minor Alastrim Para smallpox*) This form is found in South Africa America West Indies and Great Britain

The virus of alastrim is really an atenuated smallpox virus and closely allied to vaccinia because it produces the typical papulocutaneous lesions on inoculation into monkeys though it fails to do so in calves On recovery from the infection by the alastrim virus the monkey develops immunity to vaccinia

The disease is characterised by the following features

1 *Prodromata* Usually not severe if present at all

2 *Eruptions* Appear usually on the third or fourth day but occasionally may be delayed till the seventh or eighth day The vesicles are mostly unilocular and not multilocular as in typical smallpox The characteristic centrifugal distribution is however present There is the same tendency of the eruption to avoid the most protected parts and the flexures of the body such as lower abdomen axillæ and groins

3 *Fever* Secondary fever is absent except in rare cases

4 *Complications* Rare

5 *Mortality* Extremely low

6 Alastrim never reverts to the classical type of smallpox

DIAGNOSIS

During an epidemic the diagnosis of mallpox is rather easy but difficulty arises in the diagnosis of sporadic cases A consideration of the following data is essential

CLINICAL DATA 1 Absence of scars of succes ful vaccination in the past

2 Sudden onset of high fever with a temperature of 103° 105 F

3 Presence of rigor inten e headache severe backach and prostration

4 Flu hed appearance

5 Pre ence of vomiting

6 Occasional presence of petechial ra h in the lower abdomen groins and axillæ

7 Appearance of a maculo papul ir erup ion with the shotty feel on the third or fourth day with the characteristic centrifugal distribution and the subsequent evolution The eruptions are more numerous on face hands and legs than on abdomen back and ch st They do not invade the axillæ and groins The fall of the temperature to normal on the appearance of the rash is an important guide to the diagnosi

LABORATORY DATA 1 Examination of the blood in the pre eruptive stage shows moderate leucocytosis (15 20 000 per c mm) with lymphocytosis and neutropenia

2 Examination of scrapings from the eruption In the early papular and vesicular stage of smallpox specifi elementary bodies in large numbers can be demonstrated in films of scrapings from the cutaneous or mu ous lesions These films are mordanted and stained with carbol fuchsin Elementary bodie of chicken pox are smaller (0 125 to 0 175 μ) scantier and very difficul to stain and can thus be easily differentiated from tho e of smallpox which are larger (0 25 0 4 μ) and are readily recognised A pos tive diagnosis could thus be m ide by Van Rooyen and Illingworth in 96 per cent cases

3 Complement fixation test with antigen prepared from crusts

4 Inoculation into chorioallantoi membrane of developing chick embryo

5 Inoculation of a rabbit s cornea with materials from the eruptions of mallpox give rise in 48 hours to a ve icular eruption The histological examination of the excised cornea shows the Guarnie i bodies in the epithel al ce l This test (Paul s t st) is of value in the differentiation of smallpox from chickenpox But uch a t t is of no

SEQUELÆ

1 Marked pitting and scarring of the face especially in the confluent types 2 Blindness 3 Deafness 4 Osteomyelitis frequently pyogenic less frequently necrosing and non suppurative interfering with the growth of the bones by destroying the epiphyseal lines 5 Chronic nephritis—occasionally 6 Psychoses which usually end in recovery though permanent dementia may sometimes occur 7 Alopecia occasionally

PROGNOSIS

The prognosis depends on a number of factors such as

CHARACTER OF THE EPIDEMIC The mortality varies widely in the different epidemics

HISTORY OF PREVIOUS VACCINATION AND ITS AGE In an unvaccinated community the mortality varies from 40 to 60 per cent It is exceptionally high in children Amongst the vaccinated persons the disease if it occurs at all is of the abortive or modified form Presence of well marked scars of successful vaccination in the past is of good prognostic significance

CHARACTER OF THE PRODROMATA With severe prodromal symptoms the clinical course is likely to be severe The presence of petechial rash in this stage may herald the onset of the hæmorrhagic form and is thus of grave significance

CHARACTER AND EXTENT OF THE ERUPTION In the confluent and particularly the hæmorrhagic forms the prognosis is very bad In the former type death occurs usually on the 11th or 12th day either from exhaustion due to prolonged suppuration and high fever or from shock due to peeling off of the skin producing an extensive raw surface In the latter type death occurs very early on the first to third day from toxæmia and cardiac failure

GENERAL CONSTITUTION OF THE INDIVIDUAL The prognosis is bad in the debilitated and intemperate subjects

PRESENCE OF UNFAVOURABLE SYMPTOMS AND COMPLICATIONS These render the prognosis grave

(a) Severe toxæmia associated with high and prolonged fever restlessness delirium coma and unduly rapid pulse

(b) Laryngeal involvement pneumonia and broncho pneumonia

(c) Sepsis

2 Fever is absent or of a low remittent type for five to six days with exacerbations during each fresh crop of eruptions

3 Eruptions appear on the first day of the disease and vesicles form from the very beginning which may dry up in 24 hours Successive crops appear for five to six days thus giving rise to the polymorphic character The papular stage is short and often passes unnoticed

The vesicles are superficial unilocular domeshaped and crenated at the margins The distribution is centripetal *i e* first appears on the trunk and then on the extremities The eruptions are seen equally well on extensor and flexor surfaces and protected areas of the body They are more profuse on the trunk than on the face and often absent on the hands and feet

4 Absence of severe complications and sequelæ as a rule Pitting is occasional and slight

MEASLES 1 Presence of oculo naso pharyngeal catarrh and Koplik s spots 2 Exacerbation of the temperature with the appear ance of the eruption 3 Blotchy crescentic maculopapular rash appearing on the forehead along the hairy margins and behind ears

PUSTULAR SYPHILIDES 1 History of exposure to syphilitic infection or presence of a primary sore 2 Polymorphic character of the syphilides Scaly coppery papules vesicles and pustules are seen together 3 Characteristic symmetrical distribution mostly on flexor surfaces associated with few or no eruptions on the face 4 Absence of itching 5 A longer course 6 Positive Wassermann reaction

TYPHUS 1 Rash is often absent on the face 2 Presence of typical mulberry rash on abdomen

IMPETIGO CONTAGIOSUM 1 The asymmetrical distribution on the face and hands 2 Presence of scattered cru ts and thin walled vesicles 3 Absence of lesions in the mucous membranes

DRUG RASH 1 Absence of the characteristic remission of temperature to normal on appearance of the ra h 2 Polymorphic character 3 Presence of urticarial wheals 4 History of drug administration

ACNE VULGARIS 1 Chronic afebrile disease 2 Distribution over face shoulders upper part of the back and front of the chest 3 Presence of comedones (blackheads) and scars 4 Absence of vesicular lesions

Hæmorrhagic Small Pox should be differentiated from toxic

value at the bedside for an early diagnosis in the pre eruptive stage. This and the host of other tests *viz* flocculation test precipitin test, complement deviation test are useful only in confirming or disproving the diagnosis retrospectively

DIFFERENTIAL DIAGNOSIS

In the invasive period it has to be differentiated from the following

MALARIA 1 Presence of pallor and icteric conjunctivæ 2 Presence of the malaria parasites in the blood smear

INFLUENZA 1 Presence of the oculo nasal catarrh 2 Signs of pharyngitis 3 Relative bradycardia 4 Leucopenia

PNEUMONIA 1 Presence of pain in the chest suppressed cough with rapid shallow respiration 2 Presence of lung signs

MEASLES 1 Presence of coryza and conjunctival catarrh 2 Appearance of Koplik s spots on the second day of the disease

CEREBROSPINAL MENINGITIS 1 The lateral decubitus with signs of meningeal irritation such as photophobia rigidity of the neck muscles and Kernig s sign 2 Relative bradycardia 3 Turbid or purulent cerebrospinal fluid on lumbar puncture showing meningococci on smear and culture

DENGUE 1 Relative bradycardia 2 Leucopenia with relative increase of lymphocytes

SCARLET FEVER 1 Extreme rarity of the disease in the tropics 2 Presence of tonsillitis and punctate erythema of the soft palate 3 Persistent punctate erythematous rash on the skin which has a wider distribution and not confined to axilla lower abdomen and groin 4 Presence of circum oral pallor 5 Presence of the typical furred strawberry tongue

In the eruptive stage smallpox is to be differentiated from the following

MOSQUITO BITE In the tropics where mosquitoes are numerous this condition causes good deal of confusion with early papular stage particularly because the face and the arms are the common sites of bites Absence of fever smallness in size of lesions and history of being exposed to mosquito bites will help in differentiating the condition In some cases it may be possible to give a diagnosis only after observation for a day or two

CHICKENPOX (*Varicella*) 1 Prodromata are slight or absent

VOMITING It may be obstinate and may persist till the appear ance of the papular eruption 1 Pieces of ice to suck 2 Intraven ous injection of 50 c cm of 25 per cent glucose solution to prevent ketosis and dehydration 3 Chlorpromazine 25 50 mg may be administered with advantage

DELIRIUM AND RESTLESSNESS 1 Hydrotherapy an essential preliminary 2 Use of sedatives *e g* chloral hydrate and bromides in doses of gr 20 each 3 Subcutaneous injection of sodium luminal gr 3

CIRCULATORY FAILURE (See page 263)

ERUPTIVE LESION *Papular stag* 1 Hairs of the scalp should be cut short especially in case of confluent eruptions on the scalp 2 Constant application of a lint mask soaked in glycerin or 2 per cent carbolic lotion over the face and lints similarly soaked may be applied over other parts of the body

Pustular Stage 1 Bandaging of hands to prevent scratching di comfort and a mildly antiseptic oily preparation (*vide infra*) has a soothing effect and also helps in the separation of scabs This body oil should be applied liberally on the skin

R/

Acidum salicylicum	gr	60
Acidum boricum	gr	120
Menthol	gr	60
Thymol	gr	60
Oleum eucalypti	min	120
Oleum olivæ	pint	1

3 Sulphathiazole or sulphadiazine given orally in standard dosage Antibiotics are useful in controlling this stage

Stage of Decrustation 1 Mask of thin linseed poultices over the face

2 Warm alkaline baths (6 ounces of sodium carbonate to 30 gallons of water)

SCARRING Various methods of treatment as outlined above have been directed towards prevention of pitting No method has been successful Painting of the face hands and other parts of the body with 5 per cent solution of potassium permanganate 3 to 4 times a day till the stage of decrustation has been advocated Liquor iodi mitis pure or diluted has also been used for painting the face and

purpura which is characterised by absence of toxæmia eruptions and flush Differentiation may also be necessary from acute leukæmias

GENERAL MANAGEMENT

The patient should be confined to bed under a mosquito net and isolated at home or in a special hospital The room is to be well ventilated and kept cool The bedclothes should be light. Tepid sponging twice a day is essential The eyes are washed with warm normal saline and the nostrils cleansed with an alkaline lotion and both instilled with liquid paraffin The mouth is kept clean by the use of mild antiseptics such as hexyl resorcinol solution glycothymolin or hydrogen peroxide and painted with boroglycerin A regular action of the bowels is maintained by enemata on alternate days after a preliminary opening dose of calomel followed by a saline purgative

DIET The diet should consist of milk skimmed milk barley water sago sugar and fruit juices and it should be adequate in calories vitamins and mineral salts Re adjustments in diet may have to be made according to the clinical condition of the patient

CONVALESCENCE Alkaline warm baths are helpful in softening the crusts and promoting their separation The patient is not allowed to be up and about till the skin is free from any trace of scale The use of tonics such as iron and strychnine is beneficial

SPECIFIC TREATMENT

As no specific remedy has yet been found out the treatment is mainly symptomatic

CHEMOTHERAPY It is doubtful whether the various chemotherapeutic and antibiotic drugs have any action on the general course of the disease beyond amelioration of signs and symptoms caused by secondary bacterial infections Penicillin or a broad spectrum antibiotic like aureomycin or terramycin may be used to combat the secondary infection

SYMPTOMATIC TREATMENT

HIGH FEVER 1 Application of icebags over the head 2 Tepid or cold sponging 3 Ice packs 4 Use of a diuretic and diaphoretic mixtures

HEADACHE AND BACKACHE 1 Application of icebags to the head and hot fomentation on the back 2 Use of aspirin or Dover s powder gr x 3 Injections of morphine in severe cases

Re vaccination in adults in India should be performed every year Failure of vaccination is not necessarily an indication of immunity

Methods of Vaccination 1 *Scarification* In vaccination the glycerinated calf lymph (in collapsible or capillary tubes) kept under cold storage for not more than 8 months is used Recently a bacteria free vaccine prepared by growing the virus on chick embryo membranes has been used with good results The outer aspect of the arm just below the insertion of the deltoid muscle is carefully cleansed with soap and water and then painted with ether or acetone which is allowed to dry up One drop of vaccine lymph are placed on the cleansed area one inch apart from each other and scratches are made through the drops by a sterile lancet or a needle into the deeper layers of the epidermis without causing any bleeding The lymph is rubbed over the scratched area and allowed about fifteen minutes for absorption after which the inoculated area may be covered with a sterile gauze

For a successful primary vaccination attention to the following details is essential

(*a*) The vaccine lymph must be fresh and potent Any lymph exposed to room temperature in the tropics for more than few hours loses its potency

(*b*) There should not be any trace of antiseptic left on the skin

(*c*) The lancet should be sterile but cool

(*d*) Bleeding should not be caused during scarification

2 *Intra cutaneous vaccination* It has recently been employed in America and England It is a simple economical and efficient method

Classical primary vaccination reaction *Local reactions at the site of inoculation*—Formation of a red papule on the 3rd day umbilicated vesicle with a red areola on the 5th or 6th day maximum size of vesicle on the 8th day pustule on the 9th or 10th day desiccation from the 12th day separation of the scab leaving a permanent scar by the 21st day

Recent work indicates that the development of a typical epidermal vesicle following primary vaccination is essential for the development of immunity (Henderson and McClean)

Constitutional symptoms—Fever slight or moderate on the 3rd to 8th day pain and swelling of the axillary glands may be present

In re vaccination the course is variable depending on immunity The local lesions and constitutional symptoms may be same as in the primary vaccination or an accelerated reaction with a peak between the third and the seventh day occurs which recedes earlier than the primary

hands once or twice a day for the first 8 10 days But the results are not very promising

TREATMENT OF COMPLICATIONS

KERATITIS AND CORNEAL ULCER 1 Daily washing of the eyes with warm boric acid lotions or normal saline 2 Application of an atropine (½ per cent) and iodoform (5 per cent) ointment to the eyes 3 Cauterisation with a thermocautery

LARYNGITIS Inhalation of medicated steam

ŒDEMA OF LARYNX Tracheotomy

BOILS AND ABSCESSES 1 Hot fomentations 2 Incision and drainage 3 Sulpha drugs or penicillin

PREVENTIVE MEASURES

1 Notification to the health authorities and strict isolation of patients at home or preferably in special hospitals till a complete separation of all crusts are essential This period usually varies from 4 to 6 weeks

2 Isolation of all contacts under medical supervision for 16 days They can however be released from quarantine earlier if a reaction occurs at the site of vaccination within that period showing the presence of immunity to smallpox

3 Disinfection of the patient s room clothes and articles by appropriate measures The clothes of doctors and attendants should also be disinfected The latter should wear gown cap and gloves during attendance on patients

4 Efficient vaccination and re vaccination of all contacts and of a community constitute the most important preventive measures against smallpox

VACCINATION The credit for the discovery of vaccination is due to Edward Jenner who in 1796 inoculated a boy with material derived from the vaccinal lesions of a milkmaid and rendered him immune against subsequent inoculation with smallpox material

All contacts especially the members of the infected family should be vaccinated at once Vaccination within three days of exposure to the disease prevents it if done within the next four days the disease if it occurs is modified New born babies are no exception to this rule though about 10 per cent of them are resistant to vaccination In systematic vaccination infants should be vaccinated between 3 to 6 months and children should be re vaccinated at the age of 3 years

CHAPTER II

CHICKENPOX

[Varicella Water pock Glass pock]

DEFINITION

Chickenpox is an acute specific infectious disease caused by a filterable virus and characterised by mild constitutional symptoms and a papulo vesicular eruption appearing in successive crops and showing simultaneously all the stages of development *e g* papules vesicles pustules and crusts

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is common in the tropical and temperate regions though prevalent all over the world It occurs both sporadically and also in the form of minor epidemics in schools and hospitals for children

SEASONAL PREVALENCE It is most frequently seen in the late autumn and winter

AGE SEX AND RACE INCIDENCE No age is exempt from the disease though it affects children especially between 1 to 10 years The disease is quite common amongst adults in the tropics Second attacks though rare are not unknown Both sexes are equally liable There is no racial predilection

CAUSATIVE ORGANISM It is a filterable virus akin to that of herpes zoster Chickenpox has broken out amongst contacts within 10 to 16 days of their exposure to cases of herpes zoster *Elementary bodies* similar to those seen in smallpox and vaccinia have been found in the fluid contents of vesicles A pure saline suspension of the bodies is agglutinated by the serum of convalescents from chikenpox and herpes zoster and not by the serum of smallpox convalescents

MODE OF INFECTION

The infecting agent enters the human system as in smallpox through the mucous membranes of the mouth and the upper respiratory tract as a result of *droplet infection from direct contact* with the patient who is infectious from the pre-eruptive period to the complete separation of all scabs

Human carriers or infected articles (*fomites*) may also play a role in transmitting the infection

reaction or there may be the immune reaction which is only a formation of red areola with or without papule Lastly re-vaccination may fail to take In these cases the subject should not be regarded as immune unless vaccination has been repeated with lymph whose potency has been tested by its effect on others

Contraindications—There is hardly any contraindication in the event of an exposure Otherwise vaccination should be done only when the subject is in good health Vaccination should be postponed in babies suffering from febrile condition skin diseases like eczema and impetigo tuberculosis and congenital syphilis It should not be done during a poliomyelitis epidemic

Complications of vaccination They are usually uncommon. The following may occur

1 A transient erythematous measly or sometimes urticarial rash may appear about 7 11 days after vaccination

2 Vesicular lesions on face due to scratching and auto-inoculation

3 Generalised vaccinia in which diffuse pustular eruptions appear all over the body on the 4th to 10th day is very rare except in children who are already suffering from skin diseases

4 Erysipelas cellulitis exfoliative dermatitis due to secondary pyogenic infection

5 Tetanus occasionally

6 Post vaccinal encephalo-myelitis very rare It usually occurs after primary vaccination when given at older age

Duration of immunity The immunity develops within three weeks from successful vaccination and lasts at least 3-4 years The average is 5 6 years but probably lasts for over ten years The duration of immunity is proportionate to the extent of vaccinal lesion Hence in primary vaccination insertions should preferably be four (two on each arm) or at least three Re vaccination may be done by two insertions

Vaccination by one linear insertion may be done in countries where post vaccinal encephalo myelitis occurs as a complication

A M

CHAPTER II

CHICKENPOX

[Varicella Water pock Glass pock]

DEFINITION

Chickenpox is an acute specific infectious disease caused by a filterable virus and characterised by mild constitutional symptoms and a papulo vesicular eruption appearing in successive crops and showing simultaneously all the stages of development *e g* papules vesicles pustules and crusts

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is common in the tropical and temperate regions though prevalent all over the world It occurs both sporadically and also in the form of minor epidemics in schools and hospitals for children

SEASONAL PREVALENCE It is most frequently seen in the late autumn and winter

AGE SEX AND RACE INCIDENCE No age is exempt from the disease though it affects children especially between 1 to 10 years The disease is quite common amongst adults in the tropics Second attacks though rare are not unknown Both sexes are equally liable There is no racial predilection

CAUSATIVE ORGANISM It is a filterable virus akin to that of herpes zoster Chickenpox has broken out among t contacts within 10 to 16 days of their exposure to cases of herpes zoster *Elementary bodies* similar to those seen in smallpox and vaccinia have been found in the fluid contents of vesicles A pure saline suspension of the bodies is agglutinated by the serum of convalescents from chickenpox an l herpes zoster and not by the serum of smallpox convalescents

MODE OF INFECTIO

The infecting agent enters the human system as in smallpox through the mucous membranes of the mouth and the upper re piratory tract as a result of *droplet infection from dire t contact* with the pati nt who is infectious from the pre eruptive period to the complete separa tion of all scabs

Human carriers or infected articles (*fomites*) may al o ₁l) a rol in tran mitting the infection

In the eruptive stage the virus may be conveyed for short distances (12 to 15 feet) *by the air*

Accidental inoculation of the abraded skin with the varicellous material is a very rare mode of infection

PATHOLOGY

The pathological lesions comprise (1) cutaneous eruption (2) mucous membrane lesions and (3) blood changes

CUTANEOUS ERUPTIONS As in smallpox the lesion begins firstly with capillary dilatation and exudation of serum into the papillary layer followed by a colliquative necrosis of some of the superficial prickle cells Liquefaction and formation of vesicles occur The vesicles are tent shaped strands of compressed epithelial cells radiate downwards and obliquely from the roof to the broad base Inspite of this reticular structure the loculation of the vesicles is not so well defined as in smallpox neither is there an umbilication Maturation occurs less frequently but more rapidly than in smallpox Because of the superficial position of the lessions and less frequent maturation scarring is rarely seen after the heating of varicellar lesions

MUCOUS MEMBRANE LESIONS These occur as a rule simultaneously with the cutaneous eruption or may precede it and quickly ulcerate as in smallpox They are usually found in the soft and hard palates less commonly in the mouth tongue pharynx and larynx The mucous membranes of the conjuctivæ vulva vagina and prepuce may be affected

BLOOD CHANGES In the eruptive stage the blood shows a moderate leucocytosis with an increase of lymphocytes and a diminution of eosoniphils and polymorphs

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is usually 14 days though it may vary from 10 to 20 days

MODE OF ONSET *In acute Stage* Prodromal signs and symptoms are often absent especially in children In the adults mild constitutional disturbances consisting of malaise chilly sensations slight fever headache slight backache and loss of appetite may occur 24 to 48 hours before the appearance of the rash Rarely in children vomiting and convulsions may occur A transient *prodromal rash* measly in nature may sometimes appear over the trunk and less frequently the extremities Small erosions are often seen in the palate

Eruptive stage On the very first day with or without fever small red macules appear first on the skin of the trunk especially the back Then they appear on the face scalp and proximal parts of the extremities Occasionally the face may be affected first They are found over the parts covered with clothes or exposed to irritation The concavities of the body do not escape groins and axillæ are affected

In severe cases the palms and soles may be involved The mucous membrane lesions already described may appear simultaneously The distribution of the rash is characteristically *centripetal i e* it is more profuse on the trunk and back than on the distal portions of the extremities The arms show a larger number of lesions than the hands the thighs more than the ankles and feet The total number of lesions may vary from a few to several hundreds The macules develop rapidly in course of a few hours into papules and vesicles In fact maculo papular stage often passes unnoticed and *the vesicular eruption is the characteristic feature from the very beginning* It appears in successive crops for 4 to 7 days accompanied by a rise of temperature The vesicles are superficial oval crenated at the margins dome shaped (non umbilicated) unilocular and surrounded by a red areola They have a clear fluid content which soon becomes turbid or sometimes purulent on the second to third day Desiccation of the individual vesicles begins within 24 hours and may be complete in 2 to 3 days The scabs separate in 10 to 21 day leaving reddish areas on the skin but no definite scars Due to the varying age of the vesicles the eruption in chickenpox shows unlike smallpox all the stages of development at the same time viz papules vesicles pustules and crusts

Fever is mild (100° 101°F) in most cases The fever usually continues till the appearance of fresh crops ceases In others fever may be absent A temperature of 104° 105 F is rare but may occur in adults During maturation of the vesicles a secondary fever of moderate degree (101 102°F) may occur and continue for a few days

CLINICAL TYPES

They are occasionally seen only in severe cases

VARICELLA BULLOSA In this type the vesicles increase rapidly in size to form big blebs which rupture easily producing large painful raw areas

VARICELLA GANGRENOSA It is characterised by formation of punched out ulcers which spread deeply and peripherally after separation of large dark crusts and are associated with severe constitutional

disturbances high fever (104° 105°F) and lung complications It occurs usually in debilitated children and convalescents from scarlet fever measles or diphtheria

VARICELLA HÆMORRHAGICA. In this type hæmorrhages may occur either around and into the vesicles or from the mucous membranes as well

COMPLICATIONS

They are definitely uncommon The following have been reported to occur from time to time

CUTANEOUS 1 Impetigo 2 Erysipelas 3 Boils and subcutaneous abscesses due to secondary pyogenic infection 4 Gangrene —already described under special types

PULMONARY 1 Mild bronchitis and bronchopneumonia occasionally Empyema rarely 2 Laryngitis rare

HÆMATOGENOUS Pyæmia due to secondary infection with *Staphylococcus aureus*

RENAL Acute nephritis rarely occurring in children in the first and second week of the disease

NERVOUS 1 Acute disseminated encephalo myelitis rarely occurring in children in the second week characterised by sudden onset, vomiting convulsions tremors ataxia and paralysis of the limbs 2 Peripheral neuritis 3 Optic neuritis 4 Ophthalmoplegia

ARTICULAR. Arthritis occasionally in the second week

OCULAR Conjunctivitis in 8 6 per cent (*Rolleston*)

AURAL. Otitis media may occur either early or late in the disease

PROGNOSIS

Amongst the exanthematous diseases it is associated with the least mortality Death has occasionally occurred as a result of severe complications such as encephalo myelitis erysipelas gangrene and pyæmia

DIAGNOSIS

The diagnosis of chickenpox is based on the following data

CLINICAL DATA 1 History of exposure to a case of chickenpox or herpes zoster 2 Mild constitutional disturbances 3 Appearance of a vesicular eruption on the first day of the disease 4 Appearance of the eruption in successive crops 5 Polymorphic character of the eruption showing papules vesicles pustules and crusts all at the same

time 6 Centripetal distribution The eruptions are seen in the following order of decreasing density Back and trunk face scalp arms thighs hands wrists ankles and feet

The axillæ and groins in contrast to smallpox are often affected in chickenpox

LABORATORY DATA Tests for distinguishing it from smallpox are described on page 343

DIFFERENTIAL DIAGNOSIS

A severe attack of chickenpox may simulate an attack of small pox The disease has to be differentiated from the following

SMALLPOX 1 Absence of well foveated scars of a successful vaccination 2 Severe constitutional disturbances 3 The occasional prodromal groin rash 4 Appearance of the maculo-papular eruption on the 3rd to 4th day and the subsequent gradual evolution 5 The characteristic centrifugal distribution of the eruption

MEASLES 1 Presence of catarrhal symptoms and Koplik s spots 2 Distribution of rash in the body 3 Exacerbation of the temperature with the appearance of the eruption 4 Characteristic rash

PUSTULAR SYPHILIDE (See page 345)

DRUG RASH 1 Absence of the characteristic remission of temperature to normal on appearance of the rash 2 Polymorphic character 3 Presence of urticarial wheals

ACNE VULGARIS (See page 345)

URTICARIA 1 History of previous attacks 2 Lesions are chiefly papular rarely vesicular 3 Distribution over the limbs especially hands and wrists 4 Marked itching

SCABIES 1 Presence of lesions on the wrists hands buttocks and genitals 2 Absence of lesions on the face 3 Occurrence of marked itching at night

IMPETIGO CONTAGIOSA 1 Presence of crusted lesions chiefly on face and only sometimes on hands and the trunk 2 A longer course

HERPES ZOSTER 1 Distribution of vesicles corresponding to the supply of posterior nerve roots 2 Presence of severe pain preceding the eruption

GENERAL MANAGEMENT

The patient is isolated at home or in a special hospital and confined to bed for 3 weeks until the skin is completely free from crust

DIET Light nourishing liquid diet consisting of milk barley water sugar fruit juices is preferable If the appetite is good and the fever is slight a liberal diet may be allowed

CONVALESCENCE Suitable tonics containing iron and strychnine are useful

SPECIFIC TREATMENT

There is no specific treatment to control the course of the disease General and symptomatic measures form the main basis of treatment

SYMPTOMATIC TREATMENT

ERUPTIVE LESIONS 1 Hairs of the scalp should be cut short if necessary 2 Bandaging of the hands or application of light splints to fix the arms to prevent scratching and secondary infection 3 Warm baths to promote separation of the scabs 4 Application of body oil as prescribed under smallpox 5 Application of ointment containing antibiotic on secondarily infected vesicles particularly on face

ITCHING Sponging of the affected parts with 1 per cent phenolised calamine lotion

TREATMENT OF COMPLICATIONS

IMPETIGO 1 Application of boric acid poultices to remove the crusts 2 Application of dilute ointment of ammoniated mercury after the removal of crusts 5 per cent sulphathiazole ointment is probably better for this purpose

GANGRENE Antibiotics and local dressings

PREVENTIVE MEASURES

1 Isolation of the patients at home or in special hospitals for 3 weeks until the separation of all crusts According to Thomson and Gordon isolation is not necessary for more than 10 11 days

2 Quarantine of contacts for 23 days

3 Disinfection of the patient s room and articles used by him

A M

CHAPTER III

DENGUE

[Break bone fever Dandy fe er Seven day fever]

DEFINITION

It is an acute specific fever of short duration usually a seven day fever caused by a filterable virus conveyed by *Aedes ægypti* and characterised by a saddle back or biphasic type of temperature headache severe pains all over the body and an initial and a terminal rash

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It is widely distributed in the tropical and sub tropical countries The prevalence of the disease in any country depends on the mosquito condition of the locality the presence of infected persons favourable conditions of temperature and humidity and presence of susceptible persons The disease occurs sporadically in endemic areas where Stegomyia abounds throughout the year It has a tendency to spread very rapidly in a susceptible community causing the out break of an epidemic The disease is most prevalent in the West Indies and it tends to occur mostly in coast lines and deltaic and riverine areas due to the prevalence of Stegomyia mosquitoes It occurs in the Philippines Burma India Pakistan (except Sind and North West Frontier Province) Syria and Asia Minor In the tropics it may also occur at a height of 4 000 to 6 000 feet above the sea level

SEASONAL PREVALENCE An epidemic occurs generally after the rainy season but sporadic cases may occur at any time of the year when Stegomyia mosquitoes are sufficiently present It occurs mostly in June July and August High atmospheric temperature seems to be a favourable condition for the occurrence of the disease as it is most prevalent during the moist hot part of the year

AGE SEX AND RACE INCIDENCE It occurs at all ages In children the disease occurs probably in a mild form and hence often missed It occurs equally in both sexes All races are equally liable

CAUSATIVE ORGANISM The disease is caused by a filterable virus (17 25μ) conveyed from man to man by *Aedes ægypti* (*Stegomyia fasciata*) though the virus has not yet been isolated and nothing is known

DIET Light nourishing liquid diet consisting of milk barley water sugar fruit juices is preferable If the appetite is good and the fever is slight a liberal diet may be allowed

CONVALESCENCE Suitable tonics containing iron and strychnine are useful

SPECIFIC TREATMENT

There is no specific treatment to control the course of the disease General and symptomatic measures form the main basis of treatment

SYMPTOMATIC TREATMENT

ERUPTIVE LESIONS 1 Hairs of the scalp should be cut short if necessary 2 Bandaging of the hand or application of light splints to fix the arm to prevent scratching and secondary infection 3 Warm baths to promote separation of the scabs 4 Application of boric oil as prescribed under smallpox 5 Application of ointment containing antibiotic on secondarily infected vesicles particularly on face

ITCHING Sponging of the affected parts with 1 per cent phenolised calamine lotion

TREATMENT OF COMPLICATIONS

IMPETIGO 1 Application of boric acid poultices to remove the crusts 2 Application of dilute ointment of ammoniated mercury after the removal of crusts 5 per cent sulphathiazole ointment is probably better for this purpose

GANGRENE Antibiotics and local dressings

PREVENTIVE MEASURES

1 Isolation of the patients at home or in special hospitals for 3 weeks until the separation of all crusts According to Thomson and Gordon isolation is not necessary for more than 10 11 days

2 Quarantine of contacts for 23 days

3 Disinfection of the patient s room and articles used by him

A M

CHAPTER III

DENGUE

[Break bone fever Dandy fever Seven day fever]

DEFINITION

It i an acute specific fever of short duration usually a seven day fever cau ed by a filterable virus, conveyed by *Aedes ægypti* and characterised by a saddle back or biphasic type of temperature headache severe pains all over the body and an initial and a terminal rash

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION It is widely distributed in the tropical and sub tropical countries The prevalence of the disease in any country depend on the mosquito condition of the locality the presence of infected persons favourable conditions of temperature and humidity and presence of susceptible persons The disease occurs sporadically in endemic areas where Stegomyia abounds throughout the year It has a tendency to spread very rapidly in a susceptible com munity causing the out break of an epidemic The disease is most prevalent in the West Indies and it tends to occur mostly in coast lines and deltaic and riverine area due to the prevalence of Stegomyia mosquitoes It occurs in the Philippines Burma India Pal istan (except Sind and North West Frontier Province) Syria and Asia Minor In the tropics it may also occur at a height of 4 000 to 6 000 feet above the sea level

SEASONAL PREVALENCE An epidemic occurs generally after the rainy season but sporadic cases may occur at any time of the year when Stegomyia mosquitoes are sufficiently present It occurs mostly in June July and August High atmospheric temperature seems to be a favourable condition for the occurrence of the disease as it is most prevalent during the moist hot part of the year

AGE SEX AND RACE INCIDENCE It occurs at all ages In children the di ease occurs probably in a mild form and hence often missed It occurs equally in both sexes All races are equally liable

CAUSATIVE ORGANISM The disease is caused by a filterable virus (17 25μ) conveyed from man to man by *Aedes ægypti* (*Stegomyia fasciata*) though the virus has not yet been isolated and nothing is known

as to its nature The virus is present in the blood and healthy men may be infected by the intravenous injection of filtered blood taken from dengue patients within the first three days of the disease Coles has found in Giemsa stained blood films from cases of human dengue during the infective period of the disease small granules in the red blood cells or free in the plasma and regards them as causal organisms

MODE OF INFECTION

The virus enters the human body through the bite of the mosquito *Aedes ægypti* which becomes infective 15 days after biting the dengue patient during the first three days of the disease From the fifteenth day onwards the mosquito remains infectious for the rest of its life and is capable of transmitting the disease to a susceptible person. A susceptible person gets the disease about 4 to 8 days after the bite by an infected Stegomyia The disease may also be transmitted by *Aedes albopictus and Aedes tæniorhynchus* the former is the chief vector in the Philippines the latter in Florida *Aedes scutellaris* transmitted the disease to troops in New Guinea The insect itself is the main reservoir of infection Man acts as a reservoir in that his blood may infect the vector

PATHOLOGY

The nature of pathological changes is not definitely known because death is extremely rare in uncomplicated cases The post mortem findings in a few complicated cases consisted of a cloudy swelling of liver and other visceræ and a few petechial hæmorrhages in the stomach and intestines Localised inflammation of the lungs and brain and periarticular effusions have been noted in some epidemics (*Manson Bahr*) In the petechial rash only extravasation of blood is seen

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is generally 4 to 10 days in most of the cases

MODE OF ONSET 1 *Invasive Period* The onset is usually sudden and associated with intense headache chill or rigor generalised pains and acute soreness of the eyeballs especially on movement In some cases the patient may have a feeling of malaise and vague pain ache and discomfort in the body for a few hours preceding an attack

(*a*) *Fever* There is a great variation in the type of fever seen in

this disease The following types of temperature have been encountered in dengue

(i) *Saddle back type* In this type there is a sudden onset of fever which remains high (103° 105°F) for the first two or three days then there is a gradual decline of the temperature which instead of reaching the normal level suddenly shoots up again on the 4th or 5th day (Fig 35) This secondary or terminal rise is followed by a complete remission of the fever in a day or two Total duration of

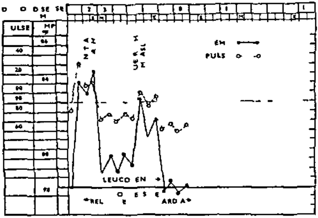


FIG 35 The saddle back type of temperature in dengue with progressive relative bradycardia

the fever is usually 6 7 days The fall of temperature to normal may be gradual or the fever may terminate abruptly with crisis of diaphoresis diuresis diarrhœa or epistaxis The first and second rises of temperature with the stage of remission in between them give the appearance of the Saddle back This is the commonest variety of the temperature curves seen in dengue

(ii) *Biphasic type* (40 per cent) This simulates the saddle back type but the primary rise of temperature drop down to normal level by the 3rd or 4th day before the occurrence of the terminal rise on the fourth or fifth day thus giving rise to a biphasic type of temperature

(iii) *Monophasic type* (31 per cent) In this the fever lasts for 2 or 3 days and then gradually declines to normal and there is no second or terminal rise of temperature

as to its nature The virus is present in the blood and healthy men may be infected by the intravenous injection of filtered blood taken from dengue patients within the first three days of the disease Coles has found in Giemsa stained blood films, from cases of human dengue during the infective period of the disease small granules in the red blood cells or free in the plasma and regards them as causal organisms

MODE OF INFECTION

The virus enters the human body through the bite of the mosquito *Aedes ægypti* which becomes infective 15 days after biting the dengue patient during the first three days of the disease From the fifteenth day onwards the mosquito remains infectious for the rest of its life and is capable of transmitting the disease to a susceptible person. A susceptible person gets the disease about 4 to 8 days after the bite by an infected Stegomyia The disease may also be transmitted by *Aedes albopictus and Aedes tæniorhynchus* the former is the chief vector in the Philippines the latter in Florida *Aedes scutellaris* transmitted the disease to troops in New Guinea The insect itself is the main reservoir of infection Man acts as a reservoir in that his blood may infect the vector

PATHOLOGY

The nature of pathological changes is not definitely known because death is extremely rare in uncomplicated cases The post mortem findings in a few complicated cases consisted of a cloudy swelling of liver and other visceræ and a few petechial hæmorrhages in the stomach and intestines Localised inflammation of the lungs and brain and periarticular effusions have been noted in some epidemics (*Manson Bahr*) In the petechial rash only extravasation of blood is seen

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It is generally 4 to 10 days in most of the cases

MODE OF ONSET 1 *Invasion Period* The onset is usually sudden and associated with intense headache chill or rigor generalised pains and acute soreness of the eyeballs especially on movement In some cases the patient may have a feeling of malaise and vague pain ache and discomfort in the body for a few hours preceding an attack

(*a*) *Fever* There is a great variation in the type of fever seen in

others it has been reported to occur in 90 per cent of case When present the rash is very diagnostic but its absence does not necessarily exclude the disease Rash is present in nearly 97 per cent of cases

Pulse rate A relatively slow pulse is a characteristic sign of dengue With the progress of the disease the pulse which is usually rapid and proportionate to the temperature at the onset tends to be slower It may be even 80 or less per minute when the temperature is 102°F or more and may be slower still 56 60 after the subsidence of the fever

Alimentary system Epigastric discomfort due to gastritis or pain in rectus muscles nausea vomiting and anorexia may be present At the height of the illness the tongue is coated with a yellowish white fur Constipation is usual but diarrhœa may appear during crisis in some cases

Lymphatic system The lymph glands especially the cervical and epitrochlear glands and less frequently the axillary and inguinal glands are often enlarged The spleen is not enlarged

Nervous system Slackness depression lack of energy and prostration are commonly seen There may be delirium during the acute stage at the height of the fever Insomnia is a common symptom perhaps due to the pain all over the body

Blood Usually it shows a progressive leucopenia in about 75 per cent of cases The white cell count may be 3000 or 4000 per c mm on the 5th or 6th day associated with lymphocytosis and neutropenia

Urinary system Urine is scanty and high coloured and may contain a trace of albumin and occasionally hyaline casts

3 *Convalescence* In most case the fever subsides by the sixth or seventh day and along with it the pains get less and gradually disappear the eruptions fade away appetite returns and steady and rapid convalescence begins Within a few days the patient feel well and strong but in some cases the pains may persist for a long time and the patient may suffer from some of the sequelæ

COMPLICATIONS

In most cases and in most epidemics the disease runs an uncomplicated course The following complications may very rarely be seen

1 Hæmorrhages from nose stomach and intestines kidneys uterus and into the retina and the skin 2 Diarrhœa 3 Bronchopneumonia 4 Collapse—occasionally seen and in most cases due to the

(*u*) *Continued type* The temperature shows little or no remission throughout the whole course of the disease This is rare

(*v*) *Abortive or Evanescent type* In this type the fever is very slight and does not last even for 24 hours

Types (*iii*) and (*v*) occur in people who have a certain amount of immunity

(*b*) *Pain* Patient usually feels severe pain all over the body especially over eye balls back loins limbs and joints (particularly the knees) There is intense frontal headache The pain and distress may be so intense that the disease fully justifies the name break bone fever The joint pain is usually periarticular being localised over the points of insertion of the muscles Though the joints are very painful still there is no swelling or any other sign of inflammation Pains which usually come on with the fever and vary in intensity with the height of the temperature render the patient unable to move even in bed from one side to the other They usually pass away with the final fall of the temperature though they may persist in some cases for a few days or weeks Pain is the most valuable diagnostic point but unfortunately like fever it is slight or even absent Absence of pain does not exclude dengue

(*c*) *Prodromal rash* A transient erythematous rash appears on the first or second day of the disease over the face neck upper part of the chest back and sometimes other parts of the body and also in the visible parts of the mucous membranes of the mouth and pharynx The conjunctivæ are usually injected This initial rash is often absent

2 *Eruptive Period* The secondary eruption which appears on the 4th to 6th day with a second rise of fever and return of the pains is the *true rash* of dengue This true rash may appear earlier and it usually lasts for one to four days It is commonly a measly rash but sometimes it may be urticarial It appears as small circular red spots first on the palms and backs of the hands The rash then quickly extends to the back chest arms and thighs and last to the legs and feet The eruptions are very thickly scattered and each spot is surrounded by an area of normal skin Sometimes the eruptions may coalesce in some places and the isolated areas of normal skin may simluate the rash The spots may be slightly elevated and may disappear on presure The eruptions disappear in order of their appearance by scaly desquamation which may continue for 2 to 3 weeks

These eruptions also like the fever and the pains are very variable In some outbreaks they are seen in a very few cases whereas in

dengue that in many cases it is difficult or impossible to differentiate Mode of onset severity of the pains temperature curve leucopenia slow pulse and tendency to attack a large number of people are remarkably similar in the two diseases Influenza shows the following characteristic features

1 Catarrhal symptoms of the respiratory tract especially marked nasopharyngeal catarrh 2 Frequent pulmonary complications

MALARIA 1 Presence of marked rigors 2 Unduly rapid pulse 3 Presence of an enlarged spleen and liver 4 Presence of malaria parasites in the blood 5 Fever responding to antimalarial therapy

MEASLES 1 It occurs mostly in children 2 Catarrhal symptoms of the respiratory tract are very pronounced 3 Koplik s spots on the second day 4 Appearance of the rash on the fourth day at the height of temperature Rash is specially marked on the face

RUBELLA 1 Presence of catarrhal symptoms of the upper respiratory tract 2 Appearance of rash on the second day

SMALLPOX (*in the pre eruptive stage*) 1 Presence of other cases of smallpox in the locality 2 Presence of rapid pulse 3 Appearance of a petechial rash on the second day over the lower abdomen groins and axillæ 4 Presence of leucocytosis

RHEUMATIC FEVER 1 The prolonged course 2 Acid sweats 3 Undue rapidity of the pulse 4 Swelling and other signs of inflammation of the big joints especially knees ankles and wrists 5 Evidences of cardiac or valvular lesions 6 Presence of leucocytosis 7 Very high erythrocyte sedimentation rate (E S R)

SCARLET FEVER 1 Very rare in the tropics 2 Pronounced signs and symptoms in the throat 3 Early appearance of the characteristic punctate erythematous rash

ENTERIC GROUP OF FEVERS The continued fever type of dengue which is very rare may sometimes be mistaken in the early stage with typhoid or paratyphoid fevers The following features are helpful in the differentiation from dengue 1 Insidious onset 2 Presence of mental apathy 3 Presence of a tumid abdomen 4 Duration of fever for more than 7 days 5 Positive hæmo culture 6 Positive Widal s test

TYPHUS FEVER (See under Typhus Fever)

YELLOW FEVER. It very closely simulates dengue In mild

administration of antipyretic drugs like aspirin phenactin quinine 5 Orchitis 6 Parotitis 7 Otitis media 8 Hyperpyrexia. 9 Skin troubles e g urticaria pruritus boils 10 Ocular palsy

SEQUELÆ

1 Insomnia 2 Depression 3 Melancholia 4 Debility 5 Persistence of pain in one or more joints 6 Relapse

Dengue offer a significantly strong immunity Repeated attacks in the same person is believed to be caused by antigenically different strains

PROGNOSIS

Mortality in uncomplicated dengue is practically nil The disease however causes a great economic loss by disabling a large number of the population of any place and thus seriously interfering with the business of the locality The severity of the disease in any epidemic varies a good deal depending upon the strain of the virus and the susceptibility of the people Hence the signs and symptoms are very variable in different places and in different outbreaks In the very young very old and debilitated persons severity of the symptoms may cause some anxiety

DIAGNOSIS

It is very easy in an epidemic but very difficult in sporadic cases In a typical case the diagnostic criteria are

1 The break bone pains 2 Saddle back type of temperature 3 Relatively slow pulse 4 The characteristic eruptions of a measly type on dorsal surfaces of hands and feet 5 Redness of the tip and edges of the tongue 6 Englarged cervial and epitrochlear glands 7 Leucopenia 8 Absence of parasites in blood smears and on culture

But if the diagnosis is based on only these features many cases of actual dengue are likely to be missed because of the variability of signs and symptoms There is unfortunately no practical specific test to arrive at a correct diagnosis which is often to be made by a process of exclusion

The method of making a definite diagnosis by transmitting the disease to human beings by experimental mo quitoes or by injecting the blood during the first three days of the disease into a susceptible individual seems to be rather impracticable

DIFFERENTIAL DIAGNOSIS

INFLUENZA An attack of influenza simulates so closely that of

CARE OF THE BOWELS A mild purgative is beneficial but no purgative should be given unless it is absolutely necessary as the muscular movement entailed by repeated defecation causes more pain and increases the suffering of the individual

CONVALESCENCE The limbs should be gently massaged or rubbed with some liniment containing opium or belladonna The use of iodides in 5 grain doses with salicylates has been recommended Return to solid food is delayed for a few days A mixture containing 20 minims of dilute hydrochloric acid and two drachms of gentian infusion is given as an appetiser The debility should be treated with good nourishing food a change to a better climate and tonics containing strychnine and iron

SYMPTOMATIC TREATMENT

FEVER 1 Cold or tepid sponging when the temperature is very high 2 Application of icebag on head—very comforting 3 An alkalinising mixture for diuresis and diaphoresis

PAIN 1 Addition of salicylates and bromides to the alkaline mixture 2 Acid acetyl salicylas or phenacetin if the pain be very intense But drugs of this group should not be indiscriminately prescribed as they are likely to produce more weakness and depression and to delay the convalescence These drugs should not be given particularly at the time of crisis 3 Hypodermic injection of $\frac{1}{4}$ or $\frac{1}{3}$ gr of morphine hydrochloride or pethidine when pain is not relieved by the above measures 4 Local application of liniments of belladonna antiphlogistin or hot fomentation

NAUSEA AND VOMITING 1 Ice to suck 2 Sips of warm water to drink 3 Calomel in fractional dose

SLEEPLESSNESS Bromide and chloralhydrate in doses of gr 20 each by the mouth

PREVENTIVE MEASURES

PERSONAL PROPHYLAXIS Patients should be kept under mosquito curtains during the first three days of the disease to prevent the spread of infection by the mosquitoes

GENERAL PROPHYLAXIS 1 During an epidemic people should lie under mosquito curtains to avoid mosquito bites 2 Measures should be taken for destruction of the Stegomyia mosquitoes and of their breeding places

P B B

attacks of yellow fever there is no point which can distinguish one from the other Both have sudden onset self limited course of same duration secondary rise of fever same incubation period similar tendency to spread transmission by the same insect and perhaps similar kind of filterable virus

1 It has not yet been reported in India though dengue is very prevalent With rapid communication by air routes at the present time there is a great chance of the infection spreading to India from persons infected in East Africa and so the possibility of yellow fever may sometimes have to be considered 2 Jaundice is a prominent feature in severe cases of yellow fever appearing on the 3rd-4th day 3 Tendency to hæmorrhages and albuminuria are very marked in yellow fever 4 Presence of leucocytosis except in mild case 5 *Yellow fever is often fatal*

SANDFLY FEVER This fever which is caused by a virus akin to that of dengue and is conveyed by sandflies *Phlebotomus papatasii* very closely resembles dengue in its mode of onset self limited course of short duration and tendency to an epidemic spread among susceptible persons and many other signs and symptoms It has the following features

1 It occurs in places where sandfly abounds 2 Terminal or secondary rise of temperature is absent 3 Rash rarely seen 4 Enlargement of glands rarely seen 5 Immunity lasts longer—for one year after the attack 6 The virus is present in the blood during first day only when the patient is capable of infecting the sandfly and not later 7 The sandfly is capable of communicating the disease to another person from the 7th or 8th day onwards after the bite

TREATMENT

There is no specific remedy for the disease which has however a self limited course of short duration The treatment is mainly symptomatic and directed towards the relief of distressing symptom

GENERAL MANAGEMENT

Patient should have absolute rest in a soft and comfortable bed and should be inside a mosquito curtain at night to avoid mosquito bite especially during the first three days of the disease

DIET Light nutritious liquid diet should be given in sufficient quantity if the patient has an appetite Plenty of water iced or plain soda water lemonade may be allowed

rabbits after a constant and fixed incubation period of 6 to 7 days This fixed virus is however not pathogenic to dogs and man The virus of rabies is resistant to extreme cold glycerine and phenol though easily killed by heat at 50°C and chemicals such as diluted formalin

MODE OF INFECTION

The virus gains entrance to the tissues of man and animals through infective saliva in one of the following ways

BITE OF INFECTED ANIMALS In India the disease is conveyed by bites of rabid dogs in about 85 per cent of cases Bites of jackals are responsible for about 14 per cent cases In the rest the infection may occur from cats horses and cows In South America the infection is transmitted to man by the bite of vampire bat It is possible that the disease may be communicated from man to man by bites

ACCIDENTAL INOCULATION This may result if a cutaneous abrasion or wound is licked by a rabid dog The saliva of such a dog is infectious four days before the development of symptoms

From the site of inoculation the virus slowly travels along the course of the peripheral nerve trunks without disturbing their function and reaches the central nervous system the cells of which are first stimulated and then depressed It is present in cerebro spinal fluid Subsequently it invades the salivary gland the pancreas and the intestinal glands by way of the nerves The blood and lymph do not play any part in the dissemination of the virus and they are not infective

PATHOLOGY

No characteristic lesions are visible to the naked eye There is congestion of the brain and spinal cord the salivary glands pancreas thyroid and suprarenal glands which may show petechial hæmorrhages Microscopically the nerve cells of the medulla the cord and less frequently the cerebral cortex show diffuse degenerative and inflammatory changes associated with marked neuroglial reaction and perivascular round celled infiltration Evidences of catarrhal inflammation may be present in all the mucous membranes

The specific lesions which are almost constantly found and have a diagnostic importance consist of the *Negri bodies* described by Negri in 1903 which are round or oval red bodies with a blue centre in the substance of the cells

The nerve cells of the hippocampus major and the Purkinje s cells of cerebellum of rabid animals show on suitable staining almost the constant presence of these *Negri bodies* 1 to 20 *microns* in diameter

CHAPTER IV

RABIES

[Hydrophobia Lyssa La rage]

DEFINITION

It is an acute specific infectious disease of short duration caused by a virus transmitted to man through infected saliva by the bite of rabid animals chiefly dogs less commonly wolves and jackals Clinically it is characterised by marked irritability anxiety and fear dysphagia moderate fever painful spasms of the pharyngeal, laryngeal and respiratory muscles induced by attempts to drink water and almost invariable occurrence of death on the 3rd to 5th day of the development of symptoms

ETIOLOGY

Geographical Distribution The disease has a world wide distribution It is very common in India where there is no strict law for the muzzling of dogs It is rare in Great Britain and Germany but occurs in France Spain Italy and Russia Australia is free from the disease

Distribution in Animals All mammals exposed to the bites of infected animals are susceptible In the tropical and sub tropical countries the disease is prevalent amongst the street dogs wolves and jackals Cats may also be affected Horses sheep and goats are also susceptible The cattle and the vampire bat in South America and the West Indies are a common source of the disease Birds especially chickens may also be affected

Seasonal Prevalence There is no particular seasonal incidence.

Age and Sex Incidence No age is immune Persons of both sexes are equally liable

Causative Organism Rabies is caused by a specific filterable virus of a neurotropic nature akin to the minute globoid bodies of poliomyelitis There are two strains of the virus (*a*) *Street virus which occurs in the nerve tissues and salivary juices of naturally* infected dogs and other animals It produces the disease in rabbits inoculated by the subdural route after an incubation period of 15 to 20 days (*b*) *Fixed virus* which is a modified form of the street virus as a result of repeated passages through rabbits brain and spinal cord until it increases in virulence and produces the disease in inoculated

due to the sudden contractions of the muscles of larynx and pharynx. Gradually the convulsions become generalised producing opisthotonos. They may be brought about by any apparent stimuli from the skin or special sense organs such as eyes and ears. The patient becomes maniacal and suffers from delusions. He does not however bite other persons. In the interval between the paroxysms he is quiet and his mind is clear. The urine often shows sugar and acetone. This stage lasts for one to three days. Death may occur from cardiac failure during paroxysms. If the patient survives this stage he passes on to the next stage.

Paralytic stage. The convulsions gradually cease leaving the patient in a state of marked exhaustion. An ascending paralysis of the extremities and trunk appears and death from coma occurs. A terminal hyperpyrexia may be present. This stage is rare in human rabies in India. It is commonly seen in rabies transmitted to man by the vampire bat.

PARALYTIC RABIES. This form is not common in man. In the Trinidad outbreak transmitted by vampire bats all the cases were of this variety. The prodromal symptoms are absent or a short prodromal stage is rapidly followed by the development of paralysis which at first involves the legs and then the trunk. The arms may or may not be affected later. There is a loss of control over the sphincters. Sensory loss may occur but it is not constant. Dysphagia is present due to bulbar paralysis and death occurs from respiratory failure.

The duration of this type of the disease is as long as 7 days whereas that of the furious type is 3 to 4 days.

COMPLICATIONS

1. Generalised convulsions. 2. Cardiac failure in the stage of excitement, very common. 3. Mania and delusions. 4. Coma. 5. Terminal hyperpyrexia. 6. Acute ascending paralysis (*Landry's type*).

PROGNOSIS

All persons who are bitten by rabid animals do not develop the disease. The chance of developing the disease after the bites of a rabid animal depends on the following factors:

1. *Nature of the biting animal.* Of the individuals bitten by rabid dogs 10 to 15 per cent develop the disease; of those bitten by wolves about 60 per cent develop it probably because of the extensive lacerations.

the exact significance of which is still debatable They were at one time thought to be protozoal in nature and called *Neurorrhyctes hydrophobiæ* Most workers hold them to be degenerative cellular reactions to the viral infection Levaditi claims them to represent a stage in the life cycle of the virus

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It varies from 6 to 90 days depending to a great extent on the site of bite It is short in cases of bites on the face head and neck, which are close to the brain and spinal cord and richly supplied with nerves It is long in cases of bites on the legs because the route to the central nervous system is long

The average period is one to two months The chance of developing the disease after three months of the bite is less We have however seen one case with an incubation period of four months and a half and another with an incubation period of about six month

CLINICAL TYPES

According to the predominating symptoms two main clinical types are met with (1) *Furious (excited) rabies* due to irritation of the cells of the central nervous system and (2) *Paralytic (dumb) rabies* due to degeneration in the nerve cells

Mixed and atypical types may also be seen

MODE OF ONSET The onset is usually sudden Prodromal symptoms may sometimes be present

FURIOUS RABIES It is the commonest type in man and is characterised by three clinical stage

Prodromal stage The prodromal symptoms consist of

(*a*) Local pain and signs of irritation at the site of the bite *e g* tingling numbness and itching (*b*) Constitutional symptoms such as lassitude slight fever rapid pulse (*c*) Nervous symptoms *e g* restlessness insomnia anxiety and fear muscular twitchings of the limbs dysphagia hyperacusis and hyperæsthesias This stage lasts for about 2 days In some cases it may be absent

Stage of excitement The symptoms of the prodromal stage are aggravated There may be moderate fever Hydrophobia develops as a result of the violent painful spasms of the muscles of deglutition and respiration which are induced not only by attempts to drink water but also its sight The mouth is dry and the saliva is thick and viscid The voice is hoarse The patient may make odd sounds which are

due to the sudden contractions of the muscles of larynx and pharynx Gradually the convulsions become generalised producing opisthotonos They may be brought about by any apparent stimuli from the skin or special sense organs such as eyes and ears The patient becomes maniacal and suffers from delusions He does not however bite other persons In the interval between the paroxysms he is quiet and his mind is clear The urine often shows sugar and acetone This stage lasts for one to three days Death may occur from cardiac failure during paroxysms If the patient survives this stage he passes on to the next stage

Paralytic stage The convulsions gradually cease leaving the patient in a state of marked exhaustion An ascending paralysis of the extremities and trunk appears and death from coma occurs A terminal hyperpyrexia may be present This stage is rare in human rabies in India It is commonly seen in rabies transmitted to man by the vampire bat

PARALYTIC RABIES This form is not common in man In the Trinidad outbreak transmitted by vampire bats all the cases were of this variety The prodromal symptoms are absent or a short prodromal stage is rapidly followed by the development of paralysis which at first involves the legs and then the trunk The arms may or may not be affected later There is a loss of control over the sphincters Sensory loss may occur but it is not constant Dysphagia is present due to bulbar paralysis and death occurs from respiratory failure

The duration of this type of the disease is as long as 7 days whereas that of the furious type is 3 to 4 days

COMPLICATIONS

1 Generalised convulsions 2 Cardiac failure in the stage of excitement very common 3 Mania and delusions 4 Coma 5 Terminal hyperpyrexia 6 Acute ascending paralysis (*Landry's type*)

PROGNOSIS

All persons who are bitten by rabid animals do not develop the disease The chance of developing the disease after the bites of a rabid animal depends on the following factors

1 *Nature of the biting animal* Of the individuals bitten by rabid dogs 10 to 15 per cent develop the disease of those bitten by wolves about 60 per cent develop it probably because of the extensive lacerations

2 *The depth of the bite and the number of tooth marks* If the bites are deep and several they are more likely to predispose to the disease

3 *Site of the bite* Bite on the face head and neck is followed by a rapidly developing disease which often proves fatal because of the close proximity to the brain

4 *Character of the immediate local treatment* Prompt cauterisation with fuming nitric acid kills the virus in the superficial bite and inhibits the development of the disease

5 *Preventive inoculation and the date of its commencement*

Death is almost invariable in fully developed cases of rabies Most cases of death occur within two months of the bite

DIAGNOSIS

The diagnosis of human rabies may be made from a consideration of the following data

1 History of a recent or a past bite by a rabid animal 2 Presence of great mental excitement 3 Spasms of the muscles of deglutition and respiration on attempting to drink water

DIFFERENTIAL DIAGNOSIS

Rabies has to be differentiated from the following

TETANUS 1 Incubation period is shorter *i e* usually 2 to 3 weeks 2 Presence of trismus and convulsions which are more tonic than clonic 3 Absence of spasms of the muscles of deglutition and respiration on attempts to drink water

HYSTERIA (*Lyssophobia*) 1 History of hysterical manifestations in the past 2 Development of the symptoms earlier than the usual time 3 Absence of a true pharyngeal spasm 4 Amenability to suggestion

Diagnosis of Rabies in the Biting Animals When a dog or any other animal bites a man it is important to decide whether the animal is suffering from rabies because the institution of antirabic inoculation its continuation and ultimate success depend on this decision

CLINICAL DATA Development of the following symptoms of excitement or paralysis during observation of the dog for 3 weeks

(*a*) Alteration in behaviour with perversion of appetite shown by the swallowing of pieces of paper sticks and stones (*b*) Marked excitement with tendency to run long distances and bite at various

objects and animals (c) Excessive salivation and frequent barking in a plaintive note (d) Occurrence of an ascending paralysis with dropping of the jaw and death within 3 to 4 days of the onset of symptoms

LABORATORY DATA 1 Demonstration of *Negri bodies* in the nerve cells of hippocampus major and the Purkinje s cells of the cerebellum on stained smears or sections of the brain of the killed suspected animal 2 Inoculation of the brain of a rabbit with the saliva of the suspected animal will lead to the death of the rabbit from rabies

TREATMENT

Once the disease is developed there is no remedy which can prevent the fatal outcome The value of antirabic serum is not yet proven Hence the treatment is directed towards the relief of distressing symptoms

GENERAL MANAGEMENT

The patient is confined to bed in a darkened quiet room He should be guarded against injuring himself during the convulsions

DIET It should preferably be semisolid In cases of marked dysphagia feeding by the stomach tube or rectal feeding is resorted to

SYMPTOMATIC TREATMENT

CONVULSIONS AND SPASMS 1 Rectal administration of chloral hydrate and potassium bromide gr 20 each dissolved in 4 ounces distilled water repeated at 6 hourly intervals if necessary 2 Chloroform inhalation 3 Hypodermic injection of gr $\frac{1}{4}$ of morphine hydrochloride or gr 1/100 of hyoscine hydrobromide 4 Muscle relaxants (i) *Tubarine* a stable aqueous solution of d tubocurarine chloride containing 10 mg per c cm Given intramuscularly or intravenously in the dose of 20 40 mg spasms may be successfully controlled (ii) *Myanesin* a synthetic preparation used intravenously in the dose of 10 c cm 10 per cent solution It may quickly control the spasm (iii) *Meprobamate* a synthetic preparation may be used in doses of 1 6 g—2 g either alone or in combination with phenobarbitone sodium (gr 3) with advantage

PREVENTIVE MEASURES

They are the most essential part of the treatment

PERSONAL PROPHYLAXIS *Local treatment of the wound* The successive steps are

1 Irrigation with warm saline or 1 in 1 000 solution of bichloride of mercury

2 Cauterisation of the wound and especially each tooth mark with fuming nitric acid within 48 hours of the bite

3 Application of pure carbolic acid to the bony and cartilaginous parts

4 The wound should not be closed for 3 days

Antirabic inoculation Owing to the long incubation period of rabies it is possible to produce an active immunisation even after the infection Hence the antirabic treatment is indicated under the following circumstances

Indications 1 Whenever a person is bitten by a definitely rabid animal or licked by it in the neighbourhood of a fresh cut or abrasion or even scratched by its claws

2 When bitten unprovoked by a dog which cannot be traced

3 If bitten by a jackal or wolf

4 If bitten unprovoked by a cat or a monkey

5 If the biting animal dies of an unknown cause within 10 days of its bite

6 When the biting animal is apparently well at the time of the bite but subsequently dies of rabies under the observation of experts within 10 days from the date of bite If alive at the end of this period antirabic treatment is not necessary or may be discontinued if already begun

7 In cases of bites over the face head and neck the treatment should be begun immediately and may be discontinued later if the suspected animal proves to be healthy at the end of the period of observation

8 When bitten by a man suffering from hydrophobia Human saliva may be infectious and hence antirabic treatment should be enforced Human milk or urine are not infectious So the preventive treatment is not necessary for the suckling child when the mother has been bitten by a rabid animal or is actually suffering from hydrophobia

Contra indications Practically there are no contra indications except the acute febrile disease Pregnancy in any stage does not contraindicate treatment

Method The treatment should be begun as soon as possible within a week of the bite and it consists of daily subcutaneous injections for 14 days in case of bites and 7 days in case of lick

of 5 c cm of a 1 per cent emulsion of brain tissue in 0 5 per cent carbolised saline incubated at 37°C for 24 hours (*Modified Semple's method*)

The brain tissue is obtained from sheep which have died of a fixed virus (*Paris virus*) infection The subcutaneous injection is given on the abdomen at two sites *i e* half the dose is injected on either side of the middle line Immunity is fully developed 4 to 5 weeks after the commencement of the treatment and lasts for about a year A suspicious bite after that time calls for a new course of treatment

Complications Local sensitivity reactions characterised by itchy red swellings may appear on the 8th to 10th day of the inoculation

The following general reactions may occur in course of the anti rabic treatment from the 6th to 20th day

1 Postvaccinal encephalitis

2 Acute ascending paralysis leading to a partial or complete recovery of most patients in a few months or to death in 30 per cent

3 Transverse myelitis at the dorso lumbar region

4 Polyneuritis—the facial nerves being commonly involved

The total mortality in the treated series is 0 16 per cent as compared with an expected mortality of 16 per cent in the untreated group Risk of incurring rabies being much greater than that of incurring paralysis there is no valid argument against the institution of specific antirabic therapy

Recently concentrated hyperimmune antirabies serum combined with vaccine therapy has given better results than vaccine alone To be effective the serum must be given within 72 hours of a bite The dose is 0 5 c cm per kilogram body weight

GENERAL PROPHYLAXIS Compulsory muzzling and strict quarantine of all imported dogs for six months Killing of stray dogs and wild jackals Immunisation of pet dogs by a course of at least 5 doses of good vaccine given at least once a year

A M

SECTION VII DISEASES DUE TO VITAMIN DEFICIENCY

CHAPTER I

BERIBERI

[Kakke Polyneuritis endemica Hydrops asthmaticus Barbiers]

DEFINITION

Beriberi is a nutritional disease caused by protein deficient high carbohydrate diet lacking principally in vitamin B_1 and is clinically characterised by peripheral neuritis œdema and cardiac failure

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is common in the tropical and subtropical countries where polished rice is the staple food in the diet Thus it is prevalent in China Japan the Philippine Islands Dutch East Indies the Federated Malaya States Burma and southern parts of India

SEASONAL PREVALENCE Though the disease may occur at any time of the year it is usually seen during and after the rains in hot countries Heat and moisture seem to be favourable conditions for its occurrence

AGE SEX AND RACE INCIDENCE Breast fed infants of mothers with beriberi suffer from infantile beriberi It is not common in children below six years of age then it gradually increases up to adult life from which time it is equally common at all ages Both sexes are susceptible though the disease is more commonly seen in male Usually the disease picks up the rice eaters Europeans as a rule very seldom suffer from it excepting those who take rice in their diet

PREDISPOSING FACTORS Gastro intestinal disturbances associated with chronic alcoholism gastric carcinoma chronic dysentery ulcerative colitis and chronic intestinal obstruction may predispose to the development of the beriberi syndrome (*secondary beriberi*) Prolonged illness such as typhoid fever and malaria debilitating diseases such as diabetes mellitus the physiological stress and strain of pregnancy and lactation are also predisposing factors of secondary beriberi Increased metabolic rate in hyperthyroidism may also induce secondary hypovitaminosis

THEORIES OF CAUSATION

Feeding experiments with polished rice on fowls by Eijkman epidemiological studies by Fraser and Stanton and feeding experiments of Strong and Crowell on prisoners definitely prove that beriberi is caused by an almost exclusive use of polished white rice which is lacking in some essential substance due to removal of the outer layers (the pericarp and the embryo) of the rice grains during the process of milling The essential substance is now known as the thermolabile antineuritic vitamin B_1 (*thiamin*) soluble in water and alcohol Apart from a diet of polished rice other diets such as tinned and autoclaved food bread of white wheat flour lacking in vitamin B_1 also give rise to beriberi This is the explanation of the cases of ship beriberi or asylum beriberi The exact role of vitamin B in the production of beriberi is not yet clearly understood Aneurin or thiamin in the form of thiamin pyrophosphate forms the cocarboxylase which together with the carboxylase helps in the break down of pyruvic acid (an important intermediary product of carbohydrate metabolism) In beriberi and allied deficiency states excess of pyruvate can be detected in the blood the value rising above the normal level of 0 5 to 1 mg per cent in extreme cases values as high as 7 or 8 mg have been found Thiamin is excreted in the urine in which it may be estimated by oxidising to thiochrome and extracting with butyl alcohol

PATHOLOGY

Thus lack of thiamin lead to inefficient carbohydrate metabolism and those cells of the body which depend chiefly on carbohydrate for their energy requirement like the cells of the nervous system suffer most

Nervous System The peripheral nerves undergo degeneration specially at the distal ends They show variable changes involving medullary sheath to complete Wallerian degeneration lesions are also seen in vagus phrenic and cranial nerves and the sympathetic chain Microscopically there is degeneration of the myelin sheath and also of the cells of Schwann and in some cases complete Wallerian degeneration might be detected The muscles supplied by the affected nerves show the characteristic changes of lower motor neurone degeneration with atrophy of the muscles cloudy swelling loss of striation and diminished sarcoplasm

In the central nervous system there is some degeneration of the sheaths of the anterior and posterior nerve roots The posterior

columns of the spinal cord are also affected occasionally as also the ganglion cells of the medulla and pons

CIRCULATORY SYSTEM In the wet type the heart especially the right side including the conus arteriosus is markedly enlarged The large systemic veins are extremely conge ted and the right auricle i very much dilated The muscle fibres of the heart show intracellular œdema sarcolysis and hydropic degeneration interfering with an efficient contraction (*Wenckebach*) The liver is enlarged and has a nutmeg appearance Effusions into the subcutaneous tissues and the serou sacs such as œdema ascites hydrothorax and hydropericardium are u ually present

ALIMENTARY SYSTEM The mucous membranes of the stomach and duodenum may show congestion and petechial hæmorrhages

ADRENAL GLANDS Enlargement of the adrenal glands has been described by McCarrison who ascribes the œdema to a rai ed intra capillary pressure caused by increased adrenaline secretion

CLINICAL MANIFESTATIONS

INCUBATION PERIOD It varies from 2 3 month One of the most important features of the disea e is the variability of the sign and symptoms according to the degree of vitamin deficiency

MODE OF ONSET It is usually insidiou In some cases ga tro intestinal prodromata such as anorexia epigastric pain and di comfort nausea vomiting and occasionally diarrhœa may be pre ent In others nervous prodromata *e g* numbness and tingling of the toe and feet heaviness of the legs pain and tenderness in the calf mu cle and muscular weakness appear

The sub equent clinical course which is usually afebrile except in the early stages (when a temperature of 100 101°F is not uncommon) may be described under the following clinical type

CLINICAL TYPES

LARVAL TYPE (*Rudimentary type*) It is caused by a slight degree of vitamin deficiency and is characterised by heaviness and stiffness of the legs and the appearance of the usual nervous prodromata followed by pretibial anæsthesia diminution or loss of the ankle and later on of the knee jerks Memory is diminished and there is lack of concentration and the person may become psychoneurotic In a few cases palpitation and dyspnœa on slight exertion may be present

ORDINARY TYPE (*a*) *Wet type* (*Dropsical type*) It is u hered

in by the usual nervous prodromata such as paræsthesias heaviness of the legs patchy anæsthesias and tenderness of the calf muscles The knee jerks are increased in the early stages but lost in later stages The patient gets progressively weaker and so cannot stand from the squatting position Œdema which is somewhat firm soon appears on the feet and legs and extends upwards till the whole body is affected Palpitation tachycardia and marked breathlessness are present The heart shows marked enlargement especially of the right side The occurrence of a fœtal rhythm of the heart sounds shortening of the circulation time gallop rhythm associated with an apical systolic bruit and accentuated or split pulmonary second sound is quite common The blood pressure is low especially the diastolic pressure the venous pressure is raised Anæmia is present Ascites hydrothorax and hydro pericardium may appear Urine shows no definite abnormality except a diminished output Several factors which probably contribute to the causation of œdema are (1) failure of cellular nutrition (2) cardiac failure and (3) lowered plasma protein level No characteristic electro cardiographic changes are present It is usually of low voltage type An indefinite inverted or flattened T wave shortened P R interval and a prolongation of the Q T are occasionally found These changes are nonspecific and complete reversion to a normal electro cardiogram occurs after treatment and recovery

The disease may be mild or severe and may run a course of several weeks or months In very serious cases death occurs from cardiac failure In favourable cases œdema may disappear and the symptoms and signs of the dry type may supervene

(*b*) *Dry type* (*Atrophic or paraplegic type*) The onset is insidious and is characterised by the occurrence of the nervous symp toms described above All those symptoms are aggravated Loss of all forms of sensation occurs over the legs especially over the tibial regions and the finger tips the ankle knee and in severe cases biceps and supinator jerks are lost Foot drop occurs and produces a high steppage gait which is also ataxic due to the loss of postural sense Wrist drop may also supervene in the late stages There is a pro gressive weakness of the legs until standing from a squatting position with the hands placed over the head is not possible (*Jongkok test*) and the patient becomes bedridden The muscles of the lower limbs and in severe cases also of the upper limbs undergo marked wasting Hyperæsthesia of the calf muscles is present The sphincters are not involved Mental changes are also absent The heart is gradually

involved and shows evidence of irritability The pulse is unduly rapid, cardiac enlargement occurs and the sounds are feeble Œdema is absent In some cases œdema may however be present over the lower parts of the legs and dorsum of the feet

This type also may at any time pass on to the wet type

ACUTE CARDIAC TYPE The failure is biventricular in type It starts with the *gastro intestinal prodromata* Cardiac symptoms such as extreme palpitation precordial pain dyspnœa cyanosis rapid feeble pulse pulmonary congestion enlarged tender liver drop y and effusion into the serous cavities appear in quick succession

The left auricle may be so much enlarged as to press on the left recurrent laryngeal branch of the vagus and cause hoarseness of the voice or even aphonia Death may occur in 1 3 days from cardiac failure

INFANTILE BERIBERI It is usually found in the breast fed infants of 2 3 months The mothers usually suffer from manifest or latent beriberi This type is especially prevalent in Egypt South China Japan and the Philippine Islands and has also been reported from South India particularly Andhra Pradesh

The *acute form* is characterised by sudden onset of breathlessness cyanosis precordial pain aphonia muscular rigidity with head retraction convulsions and a rapidly fatal termination

The *chronic form* is associated with gastro intestinal disturbance such as anorexia epigastric pain nausea vomiting and diarrhœa followed by emaciation anæmia œdema absence of knee jerks and paralysis of the limbs

Beriberi may be found in association with other deficiency states *e g ship beriberi* where there is associated scurvy or *pellagroid beriberi* with associated deficiency of niacin

COMPLICATIONS

1 Sudden or gradual heart failure
2 Pulmonary œdema and œdema of the glottis
3 Paralysis of the diaphragm and the intercostal muscles
4 Effusion into the serous cavities
5 Acute dilatation of the stomach
6 Dysentery and diarrhœa
7 Scurvy a common complication
8 Intercurrent infection

PROGNOSIS

The mortality varies from 5 to 50 per cent according to the type of the disease. In *chronic dry type* the mortality is practically nil though the disease may continue as long as six months and recovery may never be complete if the nerves have already been damaged beyond repair. The disease is very amenable to treatment if it is diagnosed and treated in the early stage.

In *cardiac type* of cases with severe vomiting, marked enlargement of the heart, fœtal or gallop rhythm and signs of failure the prognosis is very grave even when energetic treatment is carried out.

Persons who have once suffered from an attack of the disease are more susceptible than those who have never suffered from it. Recently the biochemical studies in beriberi have been found to be helpful in assessing the degree of vitamin B deficiency. The amount of bisulphite binding substances chiefly pyruvic acid in the blood and cerebro-spinal fluid is increased in beriberi and is thus an index of the extent of vitamin B deficiency.

DIAGNOSIS

It should be based on the following criteria.

1. History of a dietary deficient in vitamin B_1 such as polished rice, white flour and tinned foods. 2. Occurrence of multiple cases in the same family or locality. 3. Presence of signs of polyneuritis. 4. Presence of œdema without albumin and casts in the urine. 5. Presence of cardiac failure with normal rhythm and nonspecific E. C. G. changes. 6. Adrenaline test (*Aalsmeer*). Administration of a hypodermic injection of 1 mg. of adrenaline to a patient of beriberi brings the diastolic pressure to zero, *i.e.* the auscultatory bruit will persist even after the complete decompression of the brachial artery as long as the action of adrenaline lasts. 7. Rise of blood pyruvate level above 1 mg. per cent. 8. Low blood level or urinary excretion of thiamin. 9. Saturation tests indicating deficiency of thiamin. 10. Response to thiamin.

DIFFERENTIAL DIAGNOSIS

The dry atrophic type of the disease should be differentiated form POLYNEURITIS. This may be due to one of the following.

(1) *Alcohol.* 1. History of alcoholic habits. 2. History of loss of appetite with nausea in the morning. 3. Presence of tremors and mental changes (*Korsakoff's psychosis*).

(ii) *Arsenic* 1 History of treatment with arsenical drugs 2 Pigmentation of the skin with hyperkeratosis of the palm and soles 3 Presence of gastro intestinal disturbances 4 Presence of abnormal amounts of arsenic in urine hair and skin

(iii) *Lead* 1 History of exposure to lead 2 Early appearance of wrist drop due to involvement of the musculo spiral nerve (the supinator longus escape) 3 No sensory loss 4 Presence of other signs of lead poisoning such as blue line on gums colic constipation and punctate basophilia 5 Presence of abnormal amounts of lead in blood urine and fæces

TABES DORSALIS 1 Occurrence of lightning pains 2 Presence of Argyll Robertson pupils 3 Absence of hyperesthesia of the tendo achilli 4 Ataxic gait 5 Positive Wassermann reaction of serum and cerebro spinal fluid

PROGRESSIVE MUSCULAR ATROPHY 1 The prolonged course 2 Wasting of the muscles of the upper limbs mainly in the early stages 3 Evidence of bulbar lesions 4 Presence of fibrillary tremor 5 Absence of sensory loss

The *wet type of beriberi* may be differentiated from

SUBACUTE NEPHRITIS 1 Nephritic œdema pits on pressure more readily than the œdema of beriberi 2 Scrotal œdema is more marked than in beriberi in which it is slight or absent 3 Presence of albumin and casts in the urine

CONGESTIVE CARDIAC FAILURE DUE TO CARDIOVASCULAR LESION 1 History of previous heart disease 2 Presence of organic cardiovascular lesions such as diastolic murmurs high blood pressure arteriosclerosis 3 Absence of marked œdema of the face and arm except in rare cases

EPIDEMIC DROPSY See under Epidemic Dropsy

SEVERE HOOKWORM DISEASE See under Hookworm disease

NUTRITIONAL ŒDEMA (*Famine Dropsy*) 1 History of a diet very poor in proteins vitamins and total calories 2 Rapid improvement under a high protein diet

TREATMENT

The principles of treatment consist of

(*a*) Correction of the dietary deficiency

(*b*) Maintenance of bed rest till the recovery of the muscular power and improvement in the cardiac condition

(c) Adoption of appropriate mea ures (i) to relieve distressing symptoms (ii) to maintain nutrition of the muscles and (iii) to prevent muscular contractures

GENERAL MANAGEMENT

Rest in bed is essential owing to the mu cular weakness and paralysis and the associated pre ence of myocarditis It is still more indicated in the wet type of the disease

DIET The diet should consist of adequate protein high fatty foods (fat is thiamin sparing) and should have a rich source of vitamin B

Milk fresh or lightly boiled egg yolk fi h fresh meat mammalian liver wheat red rice carrot potatoes green vegetables pea beans and tomatoes should be given The amount of carbohydrates especially rice should be restricted Polished white rice should be eliminated Yeast extract in doses of 2 4 drachms three times daily with orange or tomato juice is a useful source of vitamin B Germinating peas may also be taken Total fluid intake hould be limited to about 25 30 ounces in the wet type of beriberi associated with congestive cardiac failure no extra salt hould be taken Focal sepsis in the teeth tonsils nasal sinuse and other places should be attended to

SPECIFIC TREATMENT

Vitamin B should be administered in adequate doses to correct the deficiency In acute cases 100 mg thiamin hydrochloride hould be injected intramuscularly daily until there is definite clinical improvement The oral administration of vitamin B is not always effective becau e it may be destroyed by the ga tric juice The symptoms of over dosage are (i) herpes zoster in 1 per cent of cases appearing after 4 8 weeks of treatment (ii) giddiness sense of constriction in the throat and severe cramps after several months of treatment (iii) headache irritability insomnia tremors (iv) allergic symptoms like violent neezing œdema of the lips and eyelid and urticarial wheals When recovery sets in thiamin 5 10 mg by mouth is sufficient as a maintenance dose

SYMPTOMATIC TREATMENT

PAIN Administration of a pirin and phenacetin in suitable doses

NEURITIS Intramuscular injections of crystalline preparations of vitamin B_1

CONGESTIVE CARDIAC FAILURE 1 Absolute rest in bed,

2 Oxygen inhalation

3 Standardised tincture of digitalis m xx 6 hourly or digoxin (0 25 mg tablet) 1 tablet 6 hourly to slow down the ventricular rate to about 70 80 per minute and thus to improve the coronary and the systemic circulation In urgent cases an intravenous injection of strophanthin or ouabain gr 1/240 may be given The cardiac failure is now believed to be of the high output type Digitalis therefore may not be helpful For the same reason venesection is not to be recommended

4 Administration of saline purgatives to produce 2 3 liquid motions and thereby relieve the portal congestion

5 Use of diuretics (*a*) Mercurials 1 2 c cm intramuscularly preceded and accompanied by oral administration of half a drachm of ammonium chloride three times a day (*b*) Chlorothiazide 500 to 1000 mg a day after breakfast for three successive days in the week for 2 3 weeks

6 Paracentesis of hydrothorax and hydropericardium may be undertaken if they are present and are interfering with the circulation or respiration

Foot Drop and Wrist Drop 1 Use of splints and sand bag to support the feet to prevent overstretching of the paralysed muscle

Muscular Wasting 1 Daily massage with active and passive movement 2 Electrical stimulation of the muscles by the galvanic current may be employed when pain and tenderness have disappeared but no muscular contractures have developed Such electrical treatment is however of doubtful value

Muscular Contractures 1 Use of extension apparatus

2 Tenotomies

PREVENTIVE MEASURES

1 Avoidance of eating white polished rice or tinned meat and autoclaved foods which are deficient in vitamin B_1

2 Use of red rice or the parboiled variety with fresh vegetables such as beans peas or other legumes and also fresh fruits

3 Use of germinating peas

4 Regular use of yeast extract twice a week under conditions of living on a restricted diet

P B B

CHAPTER II

PELLAGPA

[P losis pigmento a Mal de la rosa M l lel ole]

DEFINITION

It is a chronic relapsing disease caused by ome dietetic deficiency (of the nicotinic acid and riboflavin component of vitamin B complex) clinically characterised by sorene s of the mouth diarrhœa anæmia and achlorhydria symmetrical dermatitis especially of the back of the hands and other parts of the body exposed to the sun light as ociated with neurological signs simulating those of subacute combined degeneration of the spinal cord and mental changes such as melancholia or dementia

HISTORY

The disease was first described in 1735 by Gaspar Casal a Spani h physician under the name of *mal de la rosa* It was subsequently described by an Italian physician Frapolli in 1771 under the name of pellagra (*pelle skin agra* rough) In 1871 Lombroso recogni ed that the disease occurred chiefly among the maize eaters

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is chiefly prevalent amongst the maize eating population of the world It occurs in Northern Portugal Spain Italy Roumania the Balkan States Turkev Egypt and the Southern States of America Sporadic cas s occur in the British Isles Germany China Japan and India amongst people who do not eat maize but live for prolonged periods on a restricted diet poor in proteins and vitamins Lowe reported in 1931 the first series of cases in India amongst the patients of the Leper Ho pital Hyderabad In Bengal it is not uncommon We have seen many cases of a mild type developing in association with Banti s syndrome pulmonary tuberculosis and long continued fever like typhoid fever

SEASONAL PREVALENCE The disea e occurs in different sea on in different places Cases are however usually seen in the spring

AGE SEX AND RACE INCIDENCE It may occur at any age though the adults are usually affected and young children rarely suffer from it The adult females are more frequently attacked than males There i no evidence of any true racial selectivity

OCCUPATION It is a disease especially of the classes such as agricultural labourers occupations entailing hard outdoor labour predispose to the disease

PREDISPOSING FACTORS They are same as in beriberi

CAUSATIVE FACTORS

Funk in 1912 suggested that the disease was due to some vitamin deficiency in the diet Goldberger (1915) however considered it to be caused by a deficiency of proteins as the maize the staple diet of pellagrin was poor in protein content and deficient in certain important amino acids lysine and tryptophan Wilson supported the amino acid deficiency as the cause of pellagra Tryptophan has been shown to be converted to nicotinic acid in the body Recent investigations of Goldberger and his associates on canine black tongue human pellagra and rat dermatitis showed that administration of yeast rich in vitamin B complex was effective in preventing the occurrence of black tongue in dogs pellagra in man and dermatitis in rat fed on pellagra producing diets

It is clearly evident from these experimental observations that the pellagra preventing factor (P P factor) is a part of the vitamin B complex containing (*a*) nicotinic acid (*b*) riboflavin (vitamin B$_2$) (*c*) pyridoxin (vitamin B$_6$) and other factors Later work has shown that nicotinic acid is the specific factor the administration of which prevents and promptly cures canine black tongue and human pellagra uncomplicated with neurological changes The dermatitis of rats however is not cured by nicotinic acid but by pyridoxin Pellagra is a manifestation of mixed deficiency mainly of nicotinic acid partly of riboflavin and probably also of pyridoxin In some cases there may be associated deficiency of vitamin B$_1$ giving rise to signs and symptoms of peripheral neuritis

It has been suggested that nicotinic acid neutralises the toxin produced in the maize or occasionally other cereals According to this view pellagra is caused by a toxic factor in presence of a relative or absolute deficiency of the P P factor (nicotinic acid) in the diet

PATHOLOGY

There is a marked emaciation of the whole body The pathological changes though variable according to different observers are chiefly as follows

ALIMENTARY SYSTEM The mucous membranes of the stomach and small intestine show atrophic changes associated with inflammation

and even ulceration The muscular coat is atrophied Ulcers of the large intestine are not uncommon Fatty changes are found in the liver and kidneys The spleen is atrophic and shows focal necrosis The suprarenals may show atrophy of both the cortex and medulla and sometimes hæmorrhages

SKIN The exposed parts of the skin surface show marked changes characterised by erythema œdema of malpighian layer desquamation and scaling (parakeratosis) causing roughening and pigmentation of the skin There is also thickening due to lymphocytic infiltration of the dermis the vessels of which show hyaline degenerative changes In later stages the affected areas may become atrophic

NERVOUS SYSTEM There are widespread changes in the nervous system viz. in the cerebrum midbrain pons cerebellum medulla spinal cord and the peripheral nerves These changes consist of degeneration and chromatolysis of the cells in the Betz layer Clarke's columns posterior root ganglia and in the anterior horn cells and their homologues in the medulla pons and midbrain Symmetrical degeneration is seen in the posterior columns and in the pyramidal and spinocerebellar tracts resembling subacute combined degeneration Thickening of the meninges with atrophy of the brain and hydrops of the ventricles may also be present The cerebrospinal fluid is however normal

CIRCULATORY SYSTEM The heart shows evidences of brown atrophy

BLOOD Hypochromic microcytic anæmia of varying grades is quite common Hyperchromic macrocytic anæmia is rare The total white cell count is usually normal though there is a slight relative lymphocytosis

BIOCHEMICAL FINDINGS A true achlorhydria (post histamine anacidity) is present in 50 per cent of the cases but the intrinsic factor of Castle is present in the gastric juice There is an increased excretion of uroresin a substance previously mistaken for coproporphyrin in the urine which however rapidly disappears under successful treatment The niacin level of blood falls and the normal daily excretion of 5 mg of niacin is also much decreased

CLINICAL MANIFESTATIONS

MODE OF ONSET The prodromal symptoms are usually referable to the gastro intestinal tract and consist of flatulence epigastric discomfort or burning sensation anorexia nausea vomiting and diarrhœa Burning pain during swallowing hot and spicy food may occur due

to stomatitis In some cases the initial symptoms may be referable to the nervous system Recurrent attacks of headache giddiness backache and arthralgia are common Listlessness and mental irritability are often present

The disease is rarely ushered in with skin lesions which usually appear weeks or months after the gastro-intestinal or nervous symptoms

In a typical case the clinical picture is characterised by the involvement of (*a*) skin and mucus membranes (*b*) gastro intestinal tract and (*c*) nervous system

SKIN The areas of the skin exposed to the rays of the sun show symmetrical erythematous dermatitis as in sun burn associated with itching or burning sensations The sites of this characteristic dermatitis are in order of frequency (i) the back of the hands in 77 per cent of cases (ii) dorsum of the feet and ankles if not covered by shoes (iii) the back of the forearms and arms (iv) legs (v) the face showing the symmetrical butterfly erythema (vi) the neck showing the formation of a collar which is however incomplete behind and (vii) the upper part of the chest

Besides these sites the dermatitis may be seen in any part exposed to friction pressure by clothing as in the arm pits elbows knee buttocks The scrotum and the vulva may rarely be affected

The affected parts show in course of about two weeks desquamation and exfoliation producing thickened rough and red patches which may later on assume especially in the dark skinned races a blackish colour Formation of blebs and crusts may occur in the affected areas Occurrence of petechiæ is not uncommon

The dermatitis undergoes remission in the late autumn or winter and recurs every year in the spring Cases of pellagra where the skin lesions are absent are not uncommon (*Pellagra sine pellagra*)

ALIMENTARY SYSTEM The patient often complains of a burning pain in the mouth and salivation during meals There are vesicles in the lips which are often atrophied The angles of the mouth are excoriated due to associated riboflavin deficiency The tongue is red atrophic and glazed due to epithelial denudation and loss of the filiform papillæ and may show aphthous ulcers near the frenum In many cases the glossitis is a late sign The gums may be swollen and bleed readily Anorexia flatulence epigastric pain nausea and vomiting may be present There is frequently diarrhœa associated with pale stools Constipation may however occur

NERVOUS SYSTEM In the early stage headache giddiness sleep lessness forgetfulness mental dullness and depression are often present Tendency to outbursts of crying is common Gradually weakness of the legs paræsthesias of the limbs tremors of the head tongue hands and fingers and athetoid movements with ataxic gait may appear The tendon jerks are at fir t exaggerated but later may dis appear The plantar responses may be exten or In short the symp toms and signs may closely resemble those of ubacute combined degeneration The signs of peripheral neuriti which may be present are due not to the pellagrous condition but due to a sociated vitamin B deficiency

Visual troubles such as dimness of vision photophobia and diplopia may occur

With further progress of the disease the occurrence of manic d pressive state and dementia in 4 40 per cent of pellagrins may necessitate removal to a lunatic asylum

Hypochromic anæmia ariboflavinosis and hypo proteinemia are associated findings

COURSE It is usually slow lasting for 2 15 years characterised by exacerbations in the spring and summer and remission in the autumn and winter

COMPLICATIONS

1 Pellagra typhus—characterised by high temperature extreme prostration muttering delirium tremors muscular rigidity and convul sions It may occur primarily as an acute form of pellagra

2 Epileptiform convulsions—rare

3 Insanity—occurs in 4 40 per cent cases of pellagra

PROGNOSIS

The mortality varies from 3 30 per cent The outlook is bad in (*a*) chronic alcoholics (*b*) aged persons (*c*) persons suffering from chronic malaria and dy entery (*d*) advanced ca es

DIAGNOSIS

The diagnosis of early and mild cases is difficult In a typical case it is based on the following data

CLINICAL DATA 1 History of residence in endemic areas 2 Occurrence of other cases in the same area 3 History of an un balanced dietary 4 Presence of glossitis and diarrhœa 5 Presence

of the characteristic symmetrical erythematous dermatitis 6 Presence of seasonal variations 8 Response to nicotinic acid therapy

LABORATORY DATA They are not helpful in the diagnosis of pellagra The laboratory investigations show

(*a*) Achlorhydria (*b*) Increase of urorosein in the urine (*c*) Decreased niacin content in blood and urine The excretion of N methylnicotinamide after a dose of 100 mg of nicotinic acid may be used as a measure of the nicotinic acid store of the body

DIFFERENTIAL DIAGNOSIS

Pellagra has to be distinguished from

SPRUE (*a*) Presence of fatty stools (*b*) Frequent macrocytic anæmia (*c*) Occasional achlorhydria

BERIBERI Presence of peripheral neuritis in the early stage

With the predominance of nervous manifestations pellagra has to be distinguished from

HYSTERIA Presence of hysterical stigmata such as pharyngeal anæsthesia stocking and glove anæsthesia monoplegias fantastic gait

GENERAL PARALYSIS OF THE INSANE (*a*) Presence of Argyll Robertson pupils (*b*) Positive Wassermann reaction of the blood and spinal fluid

The dermatitis of pellagra may simulate skin lesions such as solar dermatitis occupational dermatitis syphilitic dermatitis erythema multiforme dermatitis venenata and lupus erythematosus but it may be distinguished from them by the presence of other characteristic features of the disease especially the gastro intestinal and nervous symptoms

GENERAL MANAGEMENT

REST Rest in bed should be ensured preferably in hospitals particularly in cases of pellagra with acute mental disorders

DIET The diet should be well balanced rich in high class proteins and vitamin B complex and should supply the caloric requirement (20 per cent above normal) It should consist of fresh milk meat fish eggs liver whole wheat flour vegetables peas beans and fresh fruits Yeast extract in doses of 2 4 drachms may be given with orange or tomato juice to supply the vitamin B complex

SPECIFIC TREATMENT

Nicotinic acid therapy carried out in adequate dosage is specific against pellagra In mild cases nicotinic acid or nicotinamide tablets

50 mg each should be given 4 times a day for about a fortnight In severe cases particularly with acute mental symptoms a daily dose of 500 1000 mg by mouth 500 mg subcutaneously or 50 mg of sodium nicotinate intravenously (repeated 4 such only) is necessary Improvement such as fading of the redness of the tongue occurs within as short a period as 12 24 hours A maintenance dose of 100 mg a day should be continued till disappearance of all symptoms

The symptom of overdosage or intolerance are giddiness throbbing of the head hot burning sensation over the face and neck nausea vomiting and abdominal colic Toxic symptoms occur specially when large dosage is taken on empty stomach Amide preparations of nicotinic acid are however much better tolerated because they do not produce flushing of the skin or burning sensation of the body

SYMPTOMATIC TREATMENT

The symptomatic measures are often unnecessary under the specific nicotinic acid therapy combined with a high protein diet

DERMATITIS 1 Daily intravenous injection of 0 5 g of sodium thiosulphate 2 Dusting powders

DIARRHŒA 1 Use of a high protein diet 2 Oral administration of dilute hydrochloric acid half to one drachm 3 Use of bismuth kaolin or even Dover powder if necessary 4 Daily intra muscular injections of potent liver extract preparations for 2 3 weeks Crude preparations are more effective than refined ones due to their additional content of niacin and riboflavin

STOMATITIS 1 Applications of boroglycerin with the addition of cocaine hydrochloride gr 2 to an ounce if very painful 2 Riboflavin 10 50 mg orally for 10 days is indicated in angular stomatitis (*cheilosis*)

MENTAL SYMPTOMS Administration of bromides and luminal in adequate dosage

ANÆMIA Oral administration of ferrous sulphate gr 6 t d p c

PERIPHERAL NEURITIS Intramuscular injections of vitamin B_1 in adequate doses such as 25 mg daily for 3 weeks

PREVENTIVE MEASURES

1 Avoidance of maize or other cereals in the diet 2 Regular use of a dietary rich in protein and vitamin B complex 3 Use of a daily dose of at least 50 mg nicotinic acid under conditions known to induce hypovitaminosis Autolyzed yeast product may also be used for this purpose

J C B

SECTION VIII DISEASE CAUSED BY POISONS

SUBSECTION A VEGETABLE POISONS

CHAPTER I

EPIDEMIC DROPSY

DEFINITION

Epidemic dropsy is a disease caused by the ingestion of adulterated mustard oil occuring in an epidemic or endemic form characterised by gastro intestinal disturbance oedema especially of the lower extremities with diffuse or blotchy erythema of the skin moderate pyrexia cardiac symptoms glaucoma cutaneous pigmentation and a nodular eruption

HISTORY

The first outbreak of epidemic dropsy in Calcutta occurred in 1877 Since then numerous outbreaks occurred in Calcutta and its suburbs with varying mortality rate The name of the disease was given by McLeod at Calcutta It is often wrongly thought of as a synonym of beriberi

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is prevalent almost exclusively amongst the people who use rice and mustard oil in their dietary Thus it is common in East Pakistan W Bengal Assam Orissa North Bihar and the Uttar Pradesh Cases have also been reported from Madras Certain rice eating areas *e g* China Japan Ceylon are however free from the disease

SEASONAL PREVALENCE The disease is most prevalent in the latter part of the rainy season and immediately after *i e* in June July and August

AGE SEX AND RACE INCIDENCE It affects persons of all ages except breast fed infants who as a rule escape The maximum incidence is between the age of 20 to 40 years Both sexes are equally susceptible Contrary to the usual belief the disease affects the Bengali Hindus and the Mahomedans more or less in equal extent Europeans are not usually affected The Sikhs and the Marwaris escape though living in the affected area under conditions of over crowding and unhygienic surroundings Thus better sanitary or hygienic condition does not influence the occurrence of the disease

The middle class suffers most from the disease

THEORIES OF CAUSATION

A number of theories were advanced to explain the causation of epidemic dropsy They may be briefly summarised as (i) infection theory (ii) deficiency theory and (iii) intoxication theory The argemone oil intoxication theory is generally accepted on the basis of epidemiological studies and experimental observation on man and animals Ingestion of mustard oil adulterated with argemone oil is the cause of epidemic dropsy

ADULTERATED MUSTARD OIL THEORY Observations on feeding experiments with mustard oil in human volunteers and on localised outbreaks of the disease in a closed community indicate that it is not the mustard oil itself but an adulterant *Argemone mexicana* oil present in certain consignments of the mustard oil which is responsible for the causation of the disease Signs of epidemic dropsy were reproduced in human volunteers who ingested food cooked in argemone adulterated mustard oil More recently the disease has been produced in monkeys injected or fed with argemone oil It has also been observed that the oil is absorbed into the system when applied to the intact healthy skin of monkeys

Mustard oil is often fraudulently adulterated with argemone oil or the seeds used in the expression of the oil may be accidentally adulterated with the seeds of the weed *Argemone mexicana* The adulterated mustard oil responsible for the causation of epidemic dropsy almost always gives a positive test with nitric acid for argemone oil 5 10 c cm of suspected oil vigorously shaken for 5 minutes with an equal volume of colourless concentrated nitric acid when allowed to stand gives rise to an orange yellow colour in the acid layer in presence of argemone oil There are certain fallacies with the nitric acid test Other oils as linseed oil sesame oil mahua oil olive oil give positive reaction with nitric acid

The more delicate and specific test is ferric chloride test A positive test shows orange red precipitate which under the microscope always reveals acicular crystal It is possible to detect argemone oil upto a concentration of 0 25 per cent with this test A hydrochloric acid test has also been described recently

Lastly a toxic alkaloid *sanguinarin* has been isolated from argemone oil and its poisonous effect in white mice has been demonstrated Sanguinarine acts by blocking the sulphydryl radical of the main enzyme responsible for pyruvate oxidation It may be mentioned here that beriberi interferes with the same oxidation by a

deficiency of the coenzyme thiamin pyrophosphate In beriberi supply of thiamin restores the coenzyme and cures the condition In epidemic dropsy the main enzyme is blocked and administration of thiamin (coenzyme) is useless The characteristic orange red precipitate formed in the ferric chloride test is that of sanguinarine hydrochloride

INFECTION THEORY It was suggested by many workers that the disease had an infectious origin though the nature of the infective agent and the mode of infection are still unknown

The infection theory is supported by the following data

1 Explosive nature of its appearance 2 Dramatic way of breaking out in an epidemic form 3 Members of the same family are affected one after another 4 Endemicity 5 Short incubation period 6 Presence of pyrexia 7 A definite clear cut picture of the disease having a series of symptoms like fever cutaneous manifestation gastro intestinal disturbances all of which may be looked upon as manifestations of infection

The main objections against the acceptance of this theory are as follows

1 No organism has yet been isolated 2 The disease is not communicable from man to man This observation has however been contradicted by some workers 3 Transmission of the disease to human beings or animals has failed 4 Incubation period has not been definitely ascertained

RICE THEORY Until recently it was accepted that parboiled rice played an important role in causing the disease It was postulated that when rice is stored in a damp and hot place for a long time the grains are attacked by gram positive spore forming proteolytic bacilli of the *Vulgatus* group and show central opacities The ingestion of this diseased rice produces epidemic dropsy But experiments in the School of Tropical Medicine Calcutta failed to show the growth of any organism from the central opaque area after proper sterilisation of the surfaces of the so called diseased rice grains The alternative suggestion that a histamine like body in the diseased rice is responsible for the epidemic dropsy is negatived by failure to detect any such body in the sera of patients Moreover oral administration of large doses of histamine causes no symptoms Lastly the rice theory fails to explain the explosive outbreak of the disease in an epidemic form Besides the disease has rarely occurred among the rice eating people of Madras whereas it has been definitely known to occur among people who do not take rice

VITAMIN DEFICIENCY THEORY This theory has been abandoned It is of course quite likely that lack of vitamins in the diet may render people more susceptible to this disease and thus favour its production

MODE OF SPREAD

The disease clings to houses All the members of a family living in the same house and sharing the same food may be affected whereas the adjacent house may be free from it Doctors nurses and visitors have never been reported to contract the disease by attending patients of epidemic dropsy Persons taking the same food are affected whereas persons living in the same house but having a different supply of wholesome food are not affected

PATHOLOGY

The essential pathological lesion consists of an enormous dilatation and engorgement of the capillaries of the various organs and tissues such as deeper layer of the skin subcutaneous adipose tissues skeletal muscles omentum the mucosa and submucous tissues of the intestine appendices epiploicæ pulmonary alveoli and submucous tissues of the bronchi heart and epicardial fat liver kidneys the thyroid ovaries uterus the ciliary body and the subchoroidal connective tissues the choroid plexus of the brain the perineural sheaths of the peripheral nerves and the pia arachnoid membranes of the spinal cord The brain and the substance of the spinal cord show no change The peripheral nerves do not show any evidence of neuritis

There is no evidence of any inflammation but damage to the capillary endothelium from capillary stasis and engorgement may give rise to exudation of plasma or perivascular hemorrhage Occasionally hemorrhages may occur from rupture of the extremely dilated capillaries due to loss of support from the surrounding tissues

HEART The heart may show on naked eye examination small rose red patches resembling petechial hemorrhages due to the enormous dilatation of the vessels of the epicardium The heart is enlarged the right side more than the left It shows no evidence of degeneration such as loss of transverse striations of the muscle fibres or fatty change The muscle fibres are separated from one another and also compressed by the enormously dilated intermuscular capillaries which interfere with the nutrition of the cardiac muscle and its efficient contraction In some cases a sudden extravasation of a large amount of blood may occur into the heart muscle due to rupture

of the markedly engorged capillaries and give rise to a sudden cardiac failure. The valves show no abnormality.

SKIN. The cutaneous lesions in the early stage consist of œdema and erythema due to the subcutaneous vascular dilatation. Later on red nodules appear. They originate from the papillary blood vessels of the skin and are composed chiefly of angioblastic tissues showing an active proliferation of the endothelial cells and formation of new capillaries supported in a stroma of loose areolar and fibro-blastic tissues and covered by flattened epidermis. There is no evidence of any inflammatory cellular reaction except in presence of a secondary bacterial infection. Still later the nodules may grow bigger, rupture due to a trivial injury or increased intravascular tension and cause varying degrees of hæmorrhage. Such nodules may occur on the mucous surfaces as well, such as the lip, gums, tongue and palate.

CLINICAL MANIFESTATIONS

MODE OF ONSET. The onset is usually insidious but may be sudden at times. The premonitory symptoms may consist of one or more of the following:

1. Gastro-intestinal disturbances, such as vague abdominal pains, flatulence and diarrhœa.
2. Heaviness of the lower extremities with tingling, numbness and a sensation of tiredness in the muscles of the leg, especially on walking. Heaviness and numbness of the hands may also occur during walking (*Banerjea*).
3. Dyspnœa and palpitation on exertion.
4. Appearance of rainbow haloes around light.
5. Mild or moderate fever of an irregular type.

ALIMENTARY SYSTEM. In most cases of epidemic dropsy gastro-intestinal symptoms appear quite early. Loss of appetite, nausea or vomiting, abdominal pain and borborygmi may be present. Diarrhœa is almost a constant feature. It has been ascribed to the congestion of the intestinal mucous membrane caused by the dilatation of the vessels in the submucosa. Hypochlorhydria or achlorhydria is uncommon. The stools may occasionally contain blood. Bleeding from the gums, hæmatemesis and melæna have been reported to occur. Bleeding from piles due to rectal congestion is not uncommon.

SKIN. The gastro-intestinal symptoms are soon followed or even accompanied by œdema of the legs. In the early stages the œdema is of a solid type, preceded by or associated with an

erythema due to the subcutaneous vascular dilatation Ecchymotic patches due to a telangiectatic dilatation of the blood vessels of the subcutaneous adipose tissues may be seen over the lower part of the chest abdomen buttocks and thighs Eventually œdema deve lop and spreads beyond the knees to the thigh sacral region trunk hands and even the face The supervention of congestive *cardiac failure further aggravates the œdema The skin is somewhat* thickened and inelastic and hence not freely movable The muscles of the affected area are somewhat tender The skin over the face neck hands and feet may show a generalised pigmentation Patchy pigmen tation may be present over the forehead and malar bones Tingling numbness and muscular aches are common All these symptoms may be ascribed to a stretching of the skin and the cutaneous nerves

With the progress of the disease in course of 3 6 week from the onset red nodules varying from the size of a pin s head to that of a walnut may appear in the skin (cutaneous nodules or the so called sarcoids) These nodules appear especially over the sites of previous irritation or inflammation Their appearance and number (which may be from 1 to 100) are no index of the severity of a case They are fleshy in colour painless sessile or pedunculated No growth of hair is visible on their surface They may also appear on the mucous membranes of the cheek gums tongue palate and nose They either heal up spontaneously leaving a stain on the skin or grow bigger in size and ulcerate causing hæmorrhage which may be slight or severe A secondary pyogenic infection of the ulcerated nodules is not uncommon

CARDIOVASCULAR SYSTEM Dyspnœa and palpitation on exertion are very common complaints Precordial pain may occur with or without any relation to effort The heart shows varying degrees of enlarge ment the sounds are feeble and may show a fœtal or a gallop rhythm Systolic murmur may be heard over the apical and pulmonary areas due to the dilatation of the mitral ring and the pulmonary artery respectively The pulse is usually soft and rapid (90 140) associated with a regular sinus rhythm though a low pulse rate of even 50 per minute has occasionally been observed in the early stages Occasionally extrasystoles and still rarely auricular fibrillation may occur A shortened P R interval is not uncommon Inverted or flat T waves and low voltage QRS complexes suggestive of myocardial damage may also be present In early cases there is shortening of the circulation time due to increased velocity of blood

flow and consequently increased cardiac output. In severe cases the usual signs of right-sided congestive cardiac failure appears. Both the chambers of the heart are affected. The onset of the cardiac failure may be sudden or gradual. An acute left ventricular failure may sometimes occur as the first clinical manifestation of the disease. Hydropericardium may occur as a rare complication.

The blood pressure is frequently low with a rather high pulse-pressure. In early cases the systolic blood pressure is often slightly raised.

Blood examination shows a moderate degree of anæmia usually normocytic orthochromic but may be microcytic or macrocytic. A red cell count of about 3 millions is quite common. In most cases the leucocyte count is normal though 12 000 to 16 000 per c mm with a relative increase of the polymorphs is occasionally met with. Eosinophilia may sometimes be present. It may occasionally be a high as 30 per cent. The coagulation time is normal. The specific gravity of the blood is usually low. The total plasma proteins are found to be normal though the serum albumin is reduced and globulin raised. The uric acid content is high and the calcium content is slightly low. The non protein nitrogen is normal. The average blood cholesterol is slightly higher in acute cases and definitely so in chronic and relapsing cases. In the œdematous stage the interstitial fluid and plasma volume are increased while red cell mass is reduced.

RESPIRATORY SYSTEM. In uncomplicated cases the lungs are unaffected. But in severe cases accompanied by heart failure cough dyspnœa associated with pulmonary congestion and acute pulmonary œdema are present. Hæmoptysis may result from the pulmonary congestion. Pneumonia and bronchopneumonia may occur as terminal events. Hydrothorax is occasionally present.

NERVOUS SYSTEM. Apart from the subjective symptoms such as heaviness of the lower limbs tingling numbness and soreness the nervous system shows no other abnormality. The knee jerks are often normal though exaggeration may be present in a few cases. Objective sensory loss is absent. There is no wasting or paralysis of the muscles.

VISUAL DEFECTS. At first rainbow haloes around light are seen. The intra ocular tension gradually rises due to increased exudation of fluid from the engorged ciliary vessels and glaucoma of a primary non inflammatory type with dimness of vision appears. It may be the primary manifestation in some cases in which diarrhœa œdema and cardiac symptoms are slight or absent. The tension may be as high

as 70 100 mm of mercury the normal being 20 mm The anterior chamber is either normal or deep and not shallow as in other varieties of primary glaucoma The cornea is normal or steamy in appearance due to corneal œdema Headache is frequently present There is a gradual contraction of the visual field which may lead to blindness unless operation is undertaken to relieve the tension Sudden blindness may sometimes occur due to retinal hæmorrhage resulting from a rupture of the dilated capillaries in the choroid coat

URINARY SYSTEM In cases associated with cardiac failure the total daily output of urine is diminished Albumin is absent except in a few cases where it is present in traces There are no casts or red cell in the urine in absence of congestive cardiac failure The culture shows no growth of organisms

GENERATIVE SYSTEM Menorrhagia or metrorrhagia may be present Abortion is invariable in pregnant women between the fourth to eighth month

COMPLICATIONS

1 Cardiac failure (*a*) Acute left ventricular failure which comes on suddenly (*b*) Subacute or chronic congestive heart failure especially right sided 2 Effusion into the serous cavities 3 Broncho pneumonia 4 Enterocolitis 5 Glaucoma in 5 10 per cent cases 6 Abortion—almost invariable 7 Hæmorrhages from the mucous membranes 8 Bleeding piles 9 Hæmorrhages from the cutaneous nodules 10 Septic infection of the ulcerating nodules 11 Retinal hæmorrhage occasionally

SEQUELÆ

1 Relapses quite common 2 Blindness due to optic atrophy from an unrelieved glaucoma 3 Neurocirculatory asthenia 4 Chronic myocardial fibrosis (rarely)

PROGNOSIS

In acute cases the outlook is serious Death may occur from sudden cardiac failure in a few days In the subacute or chronic cases the disease may run a variable course of 2 3 months and terminate in one of the following ways

1 Complete recovery may occur 2 Residual symptoms such as weakness œdema of the legs and feet dyspnœa palpitation and precordial pain may persist for months with ultimate recovery 3 Congestive cardiac failure may gradually supervene

flow and consequently increased cardiac output In severe cases the usual signs of rightsided congestive cardiac failure appears Both the chambers of the heart are affected The onset of the cardiac failure may be sudden or gradual An acute left ventricular failure may sometimes occur as the first clinical manifestation of the disease Hydropericardium may occur as a rare complication

The blood pressure is frequently low with a rather high pulse pressure In early cases the systolic blood pressure is often slightly raised

Blood examination shows a moderate degree of anæmia usually normocytic orthochromic but may be microcytic or macrocytic A red cell count of about 3 millions is quite common In most cases the leucocyte count is normal though 12 000 to 16 000 per c mm with a relative increase of the polymorphs is occasionally met with Eosinophilia may sometimes be present It may occasionally be as high as 30 per cent The coagulation time is normal The specific gravity of the blood is usually low The total plasma proteins are found to be normal though the serum albumin is reduced and globulin raised The uric acid content is high and the calcium content is slightly low The non protein nitrogen is normal The average blood cholesterol is slightly higher in acute cases and definitely so in chronic and relapsing cases In the œdematous stage the interstitial fluid and plasma volume are increased while red cell mass is reduced

RESPIRATORY SYSTEM In uncomplicated case the lungs are unaffected But in severe case accompanied by heart failure cough dyspnœa associated with pulmonary congestion and acute pulmonary œdema are present Hæmoptysis may result from the pulmonary congestion Pneumonia and bronchopneumonia may occur as terminal event Hydrothorax is occasionally present

NERVOUS SYSTEM Apart from the subjective symptom such as heaviness of the lower limbs tingling numbness and soreness the nervous system shows no other abnormality The knee jerks are often normal though exaggeration may be present in a few cases Objective sensory loss is absent There is no wasting or paralysis of the muscle

VISUAL DEFECTS At first rainbow haloes around light are seen The intra ocular tension gradually rises due to increased exudation of fluid from the engorged ciliary vessels and glaucoma of a primary non-inflammatory type with dimness of vision appears It may be the primary manifestation in some cases in which diarrhœa œdema and cardiac symptoms are slight or absent The tension may be as high

periodic bouts of fever with chill and rigor 4 Presence of microfilariæ in the peripheral blood

TREATMENT

There is no specific remedy which can control the course of the disease Hence the treatment is directed mainly toward the relief of symptoms and prevention of complications

GENERAL MANAGEMENT

Absolute rest in bed is essential till the disappearance of the febrile and the cardiovascular symptoms A regular action of the bowel should be maintained by saline purgative preceded by a dose of calomel or blue pill

DIET The diet should consist of a high amount of protein and a moderate amount of fat and carbohydrate supplemented with adequate quantity of vitamins Fish egg meat milk cream bread green vegetables such as green peas beans cabbage spinach and tomato should be given Fruits such as lemons oranges papayas bananas and apples are useful sources of vitamin C which will reduce the capillary permeability Rice may be added to the diet later on during recovery *The use of mustard oil should be forbidden* and replaced by some other reliable cooking fat *e g ghee* In case of diarrhœa the diet should be liquid consisting of lime whey skimmed milk glucose and dextrimaltose and orange juice

CONVALESCENCE During convalescence and even in the early stages a climatic change to a non endemic area is very helpful Administration of general tonics containing iron and strychnine would relieve the general weakness and restore the blood picture to normal A careful watch should be kept over the visual fields in cases of glaucoma so that operative interference may not be unduly delayed

SYMPTOMATIC TREATMENT

DIARRHŒA 1 Regulation of diet

2 In case of hypochlorhydria or achlorhydria dilute hydrochloric acid half to one drachm in 4 8 ounces of water sweetened with sugar and orange juice before and during the meal should be administered

3 Bismuth carbonate or colloidal kaolin may be used if necessary

ŒDEMA 1 Rest in bed 2 Diuretics 3 Use of the tincture of Ephedra vulgaris by the mouth in doses of half to one drachm three times a day on the basis that the ephedrine component of the

The mortality rate in epidemic dropsy varies in different epidemics The average mortality is about 5 per cent

DIAGNOSIS

CLINICAL DATA 1 Occurrence of the œdema of the lower extremities preceded or accompanied by gastrointestinal disturbances in several members of the family or in several persons of the same locality

2 Presence of the characteristic solid or even pitting œdema of the legs and feet associated with diffuse or blotchy erythema of the skin

3 Presence of cardiovascular symptoms without any obvious cause such as valvular lesions of rheumatic or luetic origin and hypertension with arteriosclerosis

4 Signs and symptoms of glaucoma

5 Presence of cutaneous nodules

LABORATORY DATA Normal urinary and fæcal findings Detection of argemone oil in the cooking oil but its absence in the sample supplied does not negative the diagnosis

It should be emphasized in this connection that epidemic dropsy may co exist with other diseases such as arteriosclerotic hypertensive syphilitic or rheumatic heart disease chronic nephritis malaria dysentery hookworm disease and filaria is

DIFFERENTIAL DIAGNOSIS

Epidemic dropsy may be differentiated from the following di ea e

BERIBERI 1 Occurrence of the di ease in infants 2 Œdema in certain cases 3 Presence of peripheral neuritis 4 Response to vitamin B therapy

SUBACUTE NEPHRITIS 1 Pre ence of puffiness or œdema of the face 2 Presence of pallor 3 Presence of albumin and casts in the urine

CONGESTIVE CARDIAC FAILURE FROM HEART DISEASE 1 Presence of an obvious cause to explain the cardiac failure

SEVERE HOOKWORM ANÆMIA 1 Presence of generali ed œdema and pallor associated with a comparative sense of well being 2 Presence of pale white flabby tongue 3 Presence of hookworm ova in the stools

FILARIASIS 1 Presence of lymphadenitis and lymphangiti 2 Presence of marked thickening of the skin 3 Presence of

1 Avoidance of the use of adulterated mustard oil in the cooking of food During an outbreak of epidemic dropsy the only oil properly tested and found free from argemone should be used

2 Avoidance of sharing the food of the affected family

3 Raising of the general body resistance by a high protein high vitamin and low carbohydrate diet

4 Agriculturist should exterminate the noxious weed *Argemone mexicana* in and around a mustard plantation The millowners should carefully eliminate all noxious seeds The wholesalers and retailers of mustard oil should carefully guard against adulteration with argemone oil

J C B

tincture will maintain the peripheral capillary tone and the pseudo-ephedrine component will strengthen the muscular contraction of the heart. We have not however obtained encouraging results from its use. 4. Calcium gluconate ephedrine hydrochloride and vitamin C may be used to reduce capillary permeability and maintain capillary tone. Vitamin P (a fraction isolated from Hungarian red pepper or from lemon juice) or rutin may also be tried. The results with antihistaminic drugs are variable but occasional good response has been reported.

ACUTE PULMONARY ŒDEMA. 1. Hypodermic injection of morphine sulphate gr ¼ and atropine sulphate gr 1/100. The fear of using morphine in such cases is rather too much to be justified. Atropine may also be given intravenously.

2. Continuous inhalation of oxygen by the B.L.B. mask or intranasal catheter if the mask is not available at the rapid rate of 300-400 bubbles per minute. 3. Diuretics.

CONGESTIVE CARDIAC FAILURE. (See page 381)

ANÆMIA. Administration of suitable ferrous salts or the hematinic plastules each containing ferrous sulphate gr 5. Yeast extract may also be added.

CUTANEOUS NODULES. 1. Small ones require no special treatment because they heal up spontaneously.

2. Large pedunculated ones require surgical removal under local anæsthesia.

3. Hæmorrhage from the nodules if slight may be stopped by local pressure. If severe the loose clots may be washed away and then sterile dressings soaked in 1 in 10 000 solution of the venom of Russel's viper may be applied. In case of recurrent hæmorrhages the best method is surgical removal.

GLAUCOMA. 1. Moderate cases often respond to the medical regimen of treatment but repeated observation (including perimetry) is essential. 2. Anterior sclerectomy is indicated when there is a progressive and marked contraction of the visual fields. 3. Purgative and mercurial diuretics are of little or no value in lowering the intra-ocular tension. Recently diamox has proved to be a valuable aid in lowering the intra-ocular tension. 4. Pilocarpine or eserine is useless.

PREVENTIVE MEASURES

Adoption of efficient preventive measures and public health propaganda to avoid by all means intoxication with the argemone oil. The following measures should be adopted.

SEASONAL PREVALENCE Snake bites occur most frequently in the summer and the rains

AGE AND SEX INCIDENCE No age is immune but young adults are the common victims because they are more exposed to the bites of snakes in course of their daily activities Both sexes are equally susceptible though the males show a preponderance because of their exposed lives

MORPHOLOGY

The snakes may be *non poisonous* or *poisonous* The poisonous snakes belong to two main groups —(1) *Colubridæ* which include the king cobra and the Indian kraits (*Bungarus fasciatus*) (2) *Viperidæ* which include *daboia* or the Russell s viper (*Viperæ russelli*) of India

POISON GLANDS The poison glands of the venomous snakes correspond to salivary glands The poison is secreted by a pair of glands situated one on each side of the head below the orbit The glands are covered by muscle layers which contract during the process of the bite so that the poisonous content is pressed out along the groove or the canal of the fangs The ducts of the glands do not directly communicate with either the groove or the canal but end close to it and the venom simply flows along the channels

FANGS They are present only in venomous snakes and are of two types—grooved or canalised The fangs project downwards from the upper jaw and are curved backward *i e* towards the throat (Fig 36) They may be situated either on the anterior or on the posterior part of the upper jaw In colubrides they are small and are normally in the erect position The fangs are grooved anteriorly from base to tip The groove is not open but is covered by a membrane (*vagina dentis*) thus converting it into a sort of canal The vipers have the largest fangs measuring about 1 inch and the fangs lie horizontally when the mouth is closed standing out erect at right angles to the upper jaw only when the striking attitude is assumed The fangs of the vipers are canalised

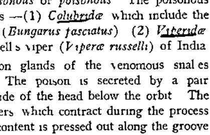


FIG 36 Showing position and direction of fangs

MECHANISM OF SNAKE BITE When a poisonous snake bites it throws itself forwards with a forcible jerk on the body opens widely

SUBSECTION B ANIMAL POISONS

CHAPTER I

SNAKE-BITE

[Snake poisoning Ophidiasis]

DEFINITION

Snake envenomation in man is caused by the inoculation of venom into the subcutaneous tissues by the bite of veniferous snakes

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The snakes both poisonous and non poisonous abound in the tropical and subtropical countries such as India Pakistan China Japan Africa Australia and tropical America.

Recently the World Health Organization published comprehensive data (*Swaroop and Grab*) regarding mortality from snake bite Total world death from snake bite is 30 000—40 000 per year Asia occupie *the first position The table below gives a comparative idea* of deaths per year for each continent

Asia	25 000—35 000
South America	3 000— 4 000
Africa	400— 1 000
North America	300— 500

In Asia largest number of deaths occurs in India where snake bite is responsible for 15 000 deaths per year A rough idea of the snake bite problem in India can be obtained from the tables collected by WHO The region of highest mortality in India lies in W Bengal where out of 387 165 deaths the average mortality from snake bite is 3 507 per year Districts lying in the Gangetic delta show more deaths than districts adjacent to the Brahmaputra delta

Annual deaths from snake bite in India

State	1945	1947	1949
Assam	30	89*	80*
Bombay	942	735	877
Madhya Pradesh	1 095	854	690
The Punjab	273	84*	128*
Uttar Pradesh	2 331	2 195	1 465
West Bengal	3 119	1 708	

* Post partition figure

rarely occurs in the pulmonary and coronary vessels and in the right side of the heart if the venom is directly inoculated into a vein during the bite

In colubrine bites the venom causes hæmolysis the blood is fluid and the right side of the heart is dilated death occurring from respiratory failure

CLINICAL MANIFESTATIONS

The clinical manifestations of snake bite vary according as (*a*) the snakes are non poisonous or poisonous and (*b*) if poisonous whether they are viperine or colubrine and (*c*) the poison injected is small or large in amount Non poisonous snake bites usually give rise to symptoms of psychical shock from fright immediately or of sepsis later on due to a secondary pyogenic infection

VIPERINE BITES *Local manifestations* The local symptoms are more prominent and severe The patient complains of severe pain and burning sensation associated with marked swelling due to hæmorrhagic exudation and constant oozing of fluid blood from the punctures (usually two) The bites are usually situated in the lower limbs or upper limbs rarely on the body face and neck

General manifestations Headache giddiness nausea and vomiting appear within 15 minutes to a few hours of the bite The temperature is subnormal Signs of peripheral failure such as coldness of the extremities cyanosis of the nose and finger tips rapid feeble pulse and markedly low bloodpressure are present The pupils are dilated and do not respond to light Coma and convulsion often supervene Petechial hæmorrhages from the various mucous membranes are frequently seen Coagulation time of the blood is increased Bleeding time may be prolonged Blood platelets may be diminished In severe case death usually occurs in 2 7 days from peripheral failure

COLUBRINE BITES *Local manifestations* The local symptoms and signs are much less marked Radiating pain along the affected limb followed by numbness at the site of bite is common

General manifestations They mainly consist of nervous symptoms such as drowsiness muscular weakness dysarthria ataxic gait and impaired sensation appearing within an hour of the bite Diplopia and ptosis are common The pupils are contracted

In severe cases there are signs of bulbar paralysis *e g* dysphagia paralysis of the tongue salivation and dysarthria Respiration gradually becomes slow and shallow the pulse is rapid and irregular

its mouth rotating forwards the upper jaw pushes in the erected fangs and then closes the jaw as a result of which the venom is squeezed into the poison duct from the venom glands and flows into the subcutaneous wound along the *grooved or canalised fangs* The closure of the jaw with adherence to the bitten area for some time is a characteristic of the elapine colubrides such as the cobra The vipers do not fix their jaws in the wound but leave the victims immediately after biting

COMPOSITION OF SNAKE VENOM The venom is a specialised salivary secretion which is a *viscid yellow fluid* slightly acid in reaction with a specific gravity of 1030-1080 In the dry state the venom consists of yellow scale which are readily soluble in water The venom has different constituents according as whether it is viperine or colubrine The *viperine venom* contains an endotheliotoxin (hæmorrhagin) which damages the capillary endothelium and produce hæmorrhages in various tissues and also some toxin which lead to a failure of the peripheral circulation with a marked fall in the blood pressure by paralysing the neuromuscular junctions of the vasoconstrictor muscles It also contains a powerful thrombokinase (occasionally thrombin) which causes intravascular clotting if it happens to enter directly into a vein during the bite The phlogogenic type of venom of daboia also contains an enzyme which helps in the formation of lysocythin locally which causes extensive local damage The elapine *colubride venom* contains (*a*) hæmolysin (*b*) several enzyme which while non toxic possess high hæmolytic property and (*c*) two types of non hæmolytic neurotoxins which cause a paralysis of the various muscles especially those of deglutition articulation and respiration by acting on the motor end plates like curare

PATHOLOGY

The main pathological lesions consist of the following

LOCAL CHANGES The bitten area especially in cases of viperine poisoning is at first swollen congested and extravasated with blood and later it shows evidence of necrosis and in some cases even of a spreading gangrene involving the whole limb The vessels in the neighbourhood may be thrombosed

SYSTEMIC CHANGES On entry into the bloodstream *via* the lymphatic vessels the viperine venom acts on the capillary endothelium of the *various organs and tissues giving rise to hæmorrhages* into the skin and from the mucous membranes into the serous sacs and in the viscera Intravascular clotting leading to sudden death

2 Identification of the type of poisonous snakes (Fig 37)

COLUBRIDAE VIPERIDAE

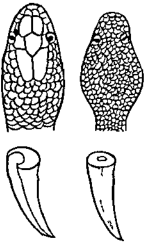


Fig 37 Showing the head and fangs of the cobra and the viper

	COLUBRIDAE	VIPERIDAE
Body	Long cylindrical	Short
Tail	Long	Short and round
Neck	Indistinct	Well defined and narrow
Head	Small oval covered with large symmetrical shield	Large pear shaped broader than body and covered with small scales
Pupils	Round	Vertical elliptical
Teeth	Small and solid on both upper and lower jaws	No small teeth
Fangs	With open groove anterior and fixed in erected position	Large fang with canal anterior and erectile

3 Presence of two or more fang marks about ½–1″ apart (Fig 38)

4 Presence of hæmorrhagic manifestations

5 Increased coagulation time of the blood

DIFFERENTIAL DIAGNOSIS

Bites of Non poisonous Snakes 1 Absence of fang marks (Fig 38) 2 Identification of the snake

and death may occur from peripheral respiratory failure associated with cyanosis coma and convulsions

COMPLICATIONS

VIPERINE BITE 1 Peripheral circulatory failure 2 Hæmorrhages into skin and from mucous membranes such as petechiæ and purpura bleeding from the gums epistaxis hæmoptysis hæmatemesis hæmaturia melæna and metrorrhagia 3 Jaundice 4 Pyogenic infection 5 Tetanus 6 Gangrene

COLUBRINE BITE 1 Peripheral respiratory failure 2 Bulbar paralysis leading to aspiration pneumonia 3 Acute ascending paralysis (Landry s type) of the spinal cord may occur after the tenth day

PROGNOSIS

The average mortality varies from 10-35 per cent The prognosis is usually influenced by (1) the nature of snake bite (viperine or colubrine) (2) the amount of inoculated poison (3) the body weight of the patient and (4) promptness of specific treatment

The mortality is almost nil in cases of bites of non poisonous snakes In very rare cases death may occur from psychical shock or secondary infection In poisonous snake bites which constitute about 40 50 per cent of all bites by land snakes (*Chopra* and *Chouhan*) the prognosis is not necessarily grave Interposition of clothing inefficient biting and inoculation of only a small amount of poison are factors which are likely to influence the prognosis favourably Bites on the head face neck and thighs are more serious than those on the feet and legs In cases where prompt and effective local treatment has not been adopted within half an hour of the bite the venom rapidly gains access to the circulation and causes death unless intravenous administration of adequate doses of antivenin is resorted to

DIAGNOSIS

The diagnosis of poisonous snake bite is made from the following data

1 History It is essential to enquire whether the snake was actually seen or killed and identified In 90 per cent of cases the identity of the particular offender is not possible because seldom are they caught the bites being more common in dark nights and without warning

TREATMENT

The main principles of treatment are to (*a*) prevent or delay absorption of the venom into the circulation by prompt adoption of efficient local measures (*b*) neutralise rapidly the venom at the site of bite (*c*) neutralise the venom that has gained access into the circulation by the intravenous administration of polyvalent antivenin in adequate doses and (*d*) relieve symptoms and treat complications as they arise

GENERAL MANAGEMENT

The patient should be confined to bed and given assurance to allay fear Warmth should be maintained by the use of blankets and hot water bags The mouth and throat should be kept free from mucus and saliva by frequent swabbing to prevent aspiration pneumonia The head should be lowered when vomiting occurs

Diet The diet should be liquid and nourishing *e g* milk barley water sugar fruit juices In case of dysphagia feeding through a Ryle s tube should be resorted to Nutrient enemata are also helpful

SPECIFIC TREATMENT

Antivenin The *intravenous* use of concentrated (usually four times) polyvalent antivenin as early as possible within 3 hours of the bite in doses of 100 c cm is highly beneficial in colubrine bites In viperine bites the results are less effective If necessary the serum administration is repeated in the same doses at the end of 8 hours The dose of antivenin is directly proportional to the time of administration and inversely proportional to the body weight A child thus requires larger doses than adults There are practically no contraindications to the use of the serum except the presence of hypersensitiveness In such cases gradually increasing desensitising doses under cover of antihistaminics should be used The local infiltration of the tissues around the bitten area with 10 12 c cm antivenin has been reported to be yielding encouraging results especially in cases of viperine bites Prompt antivenin therapy (specific or polyvalent) has reduced the mortality in snake bites

Local Measures The local measures consist of the following

Ligatur The application of ligatures which is the most important preliminary step to delay the absorption of venom is effective only when it is applied within 8 minutes of the bite (*Fairley*) One ligature over a single bone such as the femur or the humerus proximal to the bitten

POISONOUS	NON POISONOUS
Scales on the belly large and broad extending across the belly No side scale visible	Scales on belly small and similar to those on back or ventrals though broad do not stretch across Side scales visible
Spinal scales larger than the neighbouring scales and hexagonal (probably *krait*)	
Leaf shaped head with distinct neck all covered with small scales (*viper*)	Small scales on head and neck No distinct neck
Presence of pit at the side of the head	No pit
Arrow mark on head (*echis*) Neck with hood with markings (*cobra*)	
Shields on the head and third scale on the upper lip touches both eye and the nasal scale	Shields on the head but third scale on the upper lip does not touch the eye and the nasal scale
There is only one scale between eye and nose	There are two scales in between eye and nose
Fang marks ½—1 apart distinct from other rows of teeth (1 or 2) or no teeth mark but only fang marks (3)	No fang marks Marks of four rows of teeth (4)

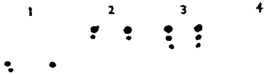


FIG 38 Shows relation between fang and teeth marks 1 2 and 3 are fang marks of poisonous snakes 4 shows only teeth marks of a non poisonous snake

RAT BITE Sometimes extreme difficulty arises when puncture marks with slight oozing of blood is present as a result of rat bite

ALCOHOLISM 1 Absence of oozing of blood from the gums or from other mucous membranes 2 Normal coagulation time of the blood 3 Absence of red cells in the urine

plasma given by slow intravenous drip method 3 Administration of adequate fluid by mouth or rectum 4 Suprarenal cortical extracts are very useful 5 Use of alcohol is contraindicated as it is not a circulatory stimulant 6 Bloodtransfusion is often very helpful

RESPIRATORY FAILURE 1 Keeping the upper air passage free from mucus 2 Artificial respiration 3 Inhalation of oxygen with 7 per cent carbon dioxide 4 Intravenous injection of 1 c cm of cardiazol ephedrine or 2 c cm of nikethamide 5 Injection of veritol (2 c cm) intramuscularly

HÆMORRHAGES 1 Administration of half to one pint of normal saline with 5 per cent glucose by the intravenous drip 2 Blood transfusion is the best Plasma may also be used 3 Injection of 500 mg of vitamin C intramuscularly or intravenously may be beneficial

SEPSIS AND GANGRENE 1 Penicillin in optimum dosage should be given 2 Adoption of appropriate surgical measures 3 Prophylactic dose of tetanus antitoxic and anti gasgangrene sera

PREVENTIVE MEASURES

1 Wearing of boots and leg guards 2 Use of lanterns and torches while going out at night 3 Avoidance of sleeping on the ground at night

L K G

area is applied to bring about a complete stoppage of circulation to the affected part Another ligature is applied a few inches distal to the bite The proximal ligature should be loosened every half an hour for about a minute to flush the limb with fresh blood and prevent necrosis The ligatures may be made with strips of clothing or preferably a rubber tubing Application of ligature is a nonspecific procedure and an adjuvant when antivenin is available but a substitute when it is not While the majority have advocated occlusion of arterial supply a few advocate application of ligature above the site of bite or above the swelling if there be any light enough to impede lymphatic flow only The ligature is to be moved ahead when the swelling advances

Incision and Mechanical Suction After the application of the ligatures the skin around the bitten area is thoroughly washed with potassium permanganate solution to remove locally deposited dried venom if there be any The bitten area is then incised to let out the venom In addition to application of ligature and incision *over* the fang marks or around them application of strong mechanical suction is also advised It is best done with a breast pump or Bier s suction glass Suction should be applied for about 20 minutes every hour for 10-15 hours Suction by the mouth which in our opinion is not a practical and safe procedure in presence of ulceration of gums cheeks and tongue is only a first aid measure

Local Venesection The distal ligature preventing venous return is left intact while the proximal arterial ligature is loosened One of the veins draining the bitten area is opened by incision and as much as half to one pint of blood is allowed to drain away One half to one third of the inoculated venom may be removed in this way This method is particularly suitable when antivenin is not available

Incision mechanical suction and venesection are extremely beneficial in case of daboia (viper) bite

Immobilisation Efforts must be made to keep the envenomated limb immobilised which can be done in spite of incision and suction

Except local injection of antivenin all other measures to destroy the toxin *in situ* should be abandoned Once a patient receives antivenin both intravenously and locally ligatures may be removed

SYMPTOMATIC TREATMENT

CIRCULATORY FAILURE 1 Application of warmth to the limbs and bandaging them 2 Intravenous administration of 5 per cent glucose or glucose saline solution Ideal therapy is 500 c cm of

PROGNOSIS

It is usually favourable though death from scorpion sting in the tropics is not uncommon in young children

DIAGNOSIS

The diagnosis may be made from the history

GENERAL MANAGEMENT

The patient should be kept in bed The bitten area should be protected against secondary bacterial infection

SPECIFIC TREATMENT

Though effective neutralisation of the circulating venom may be secured by the intravenous administration of scorpion antivenin (*Lister Institut* and *B hring Institut*) in doses of 10 c cm for adults and 5 c cm for children its use is not necessary in India

SYMPTOMATIC TREATMENT

PAIN 1 Application of a strong solution of ammonia at the site of sting to neutralise the acid poison 2 Administration of analgesic drugs like aspirin pethedine or morphine in appropriate doses 3 Local injection of 1 c cm of 2 per cent novocain gives immediate relief This may be repeated

SHOCK 1 Maintenance of warmth 2 Administration of a diffusible stimulant such as aromatic spirits of ammonia or of circulatory stimulants by the intramuscular route 3 Intravenous glucose saline or plasma in severe cases

L K G

CHAPTER II

SCORPION STING

ÆTIOLOGY

GEOGRAPHICAL DISTRIBUTION Cases of scorpion sting are frequently seen in the tropical and subtropical countries such as India China Egypt and South America

AGE INCIDENCE Children are especially liable to scorpion sting because they are ignorant of the poisonous nature of the insect and so make no attempt to avoid it

MORPHOLOGY

The scorpion has an elongated segmented body and two poison glands situated in the last segment of a flexible spined tail which is the stinging organ There are several varieties of scorpions of which the species *Buthus* or *Palamnæus* are common in India

MODE OF STING The scorpion clasps the victim with the claws and swings the tail forwards thrusting it into the skin and injecting the poison into the wound The venom is a viscid yellowish fluid faintly acid in reaction with a specific gravity of 1092 Its action is somewhat similar to that of cobra venom but much less toxic

CLINICAL MANIFESTATIONS

LOCAL The patient complains of severe pain at the site of sting which is red and swollen Signs of lymphangitis may appear

GENERAL The absorption of the poison into the circulation may give rise to systemic manifestations such as fever nausea vomiting profuse sweating and diarrhœa In children and severe cases shock muscular weakness and cramps rigidity of the muscles of the neck and jaw convulsions tremors and paralyses may be present

COMPLICATIONS

1 Secondary bacterial infection of the local wound—not uncommon 2 Coma—rare 3 Respiratory failure—rare It may be due to pulmonary œdema and paralysis of the muscles of respiration

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease is prevalent in the tropical countries such as India Iraq Syria China Australia Africa and America

SEASONAL PREVALENCE The maximum incidence occurs during May June and July the hottest months of the year in India

AGE SEX AND RACE INCIDENCE All ages are liable to the disease though men over 40 years are especially affected Males are more susceptible than females because they are more liable to be exposed to excessive heat during their heavy outdoor work Non residents in the tropics are frequently affected because of the lack of acclimatisation

PREDISPOSING FACTORS Factors which increase the production of heat in the body or interfere with the mechanism of heat loss predispose to the disease They are

1 High atmospheric shade temperature above 110 F

2 Rise in the relative humidity of the atmosphere and a wet bulb temperature above 80°F

3 Stagnation of the air and confined space

4 Heavy muscular exertion under conditions of high atmospheric temperature

5 Wearing of tight warm and ill designed clothing

7 Debilitating conditions such as overwork fatigue old age over eating chronic alcoholism and obesity affecting the efficiency of the cardiovascular system

8 Over indulgence in alcohol

9 Administration of atropine which prevents heat loss by sweating

10 Failure to acclimatise

THEORIES OF CAUSATION *Theory of Thermogenic Anhidrosis* The exposure to direct solar heat or high atmospheric temperature associated with high relative humidity and lack of air movement seriously interferes with the activity of the sweat glands Evaporation of water from body surface constitutes probably the only means of heat loss A breakdown of sweating mechanism (thermogenic anhidrosis) quickly causes a marked rise of the internal temperature of the body The excessive heat as well as the accumulated toxic products as a result of increased metabolism act directly on the various organs and tissues and give rise to the symptoms of the disease The almost constant presence of indicanuria is in favour of auto intoxication by metabolic breakdown products

SECTION IX DISEASES DUE TO PHYSICAL AGENTS

CHAPTER I

EFFECTS OF EXPOSURE TO HEAT AND SUNLIGHT

Heat is being constantly produced in the body by muscular work metabolism glandular and digestive activities all of which raise the body temperature

The loss of body heat occurs mainly through sweating evaporation of moisture from the skin and lungs radiation conduction and convection The greatest amount of heat is lost by radiation conduction and convection and about 20 per cent by evaporation The loss of heat through radiation and conduction is diminished with a rise in the temperature and relative humidity of the atmosphere Absence of moving air currents and presence of thick body clothing also hinder heat loss by radiation and convection Under such condition of high atmospheric temperature and humidity the burden of eliminating heat from the body falls mainly on the activity of the sweat glands which produce sweating and cool the body surface by abstraction of the heat during evaporation of the sweat from the skin Heat loss by evaporation however depends on the relative humidity of the air and the degree of air movement Increased humidity and diminished air movement in association with thick clothing interfere with evaporation an effective defence against rise of temperature

Exposure to excessive heat natural or artificial may under certain conditions give rise to a number of clinical syndromes namely (1) heat hyperpyrexia (2) heat exhaustion and (3) heat cramps

Heat Hyperpyrexia

[Heat stroke Sun stroke Insolation Heat fever Thermic fever Siriasis]

DEFINITION

Heat hyperpyrexia is a disease caused by continuous and prolonged exposure to the heat of the tropical sun or a high atmospheric temperature associated with a high relative humidity clinically characterised by high temperature (107° 110°F or even more) dry hot skin convulsions and coma Often a fatal termination results

and pas es into a state of coma with or without convulsions In the latter group prodromal symptoms appear a long time before the onset of the full syndrome

PRODROMAL SYMPTOMS 1 Lassitude 2 Headache and giddiness 3 Photophobia 4 Increasing thirst 5 Restlessness with mental confusion or even wild delirium 6 Frequent and painful micturition 7 Absence of sweating 8 Moderate pyrexia (100° 102°F) with a rapid pulse 9 Anorexia nausea and vomiting (common)

In course of a few hours the following manifestations appear

GENERAL The face is flushed and cyanosed pupils are contracted until just before death Skin is hot and dry The oral temperature is 108° 110°F or even more

CIRCULATORY SYSTEM Pulse is rapid and feeble The heart is dilated soft and localised apical systolic murmur may be present The bloodpressure is low due to the peripheral vasodilatation There is a relative polycythæmia with increase of hæmoglobin percentage due to marked dehydration A slight leucocytosis may be present

RESPIRATORY SYSTEM The respirations are rapid and deep often Cheyne Stokes type Lungs may also show evidence of bronchitis pulmonary congestion and œdema

NERVOUS SYSTEM Nervous manifestations are outstanding After a brief preliminary stage of restlessness and wild delirium coma sets in rapidly Pupils are contracted Muscular twitching and convulsions are frequent Deep reflexes such as the knee jerks are lost and do not re appear until convalescence is established Control of the sphincters is lost resulting in incontinence of urine and fæces

URINARY SYSTEM In ca es of dehydration the urine is scanty high coloured and shows traces of albumin red cells and a few hyaline casts Marked indicanuria is frequently present Urinary chloride is greatly reduced and in extreme cases chlorides may be absent from the urine Acetone and diacetic acid are present in 12 per cent of cases (*Manson Bahr*)

COMPLICATIONS

1 Bronchopneumonia pulmonary œdema and respiratory failure 2 Convulsions 3 Delirium 4 Shock and circulatory failure 5 Nystagmus and squint 6 Multiple neuritis

Theory of Sun traumatism It has been suggested by some authorities that sun stroke (as they prefer to call it) is the effect of some direct action of the ultra violet rays on the brain of the person exposed to the sun The main objections to this view are (1) There is no proof that the ultra violet rays can penetrate deeper than 1 5 mm into the skin and thus affect the brain and (2) heat hyperpyrexia may occur in persons who are not exposed to the sun provided the suitable predisposing atmospheric conditions are present

PATHOLOGY

Rigor mortis sets in early and decomposition occurs rapidly The brain and the meninges show evidences of marked congestion and œdema Punctiform hæmorrhages may be present The nerve cells show degenerative changes The heart is dilated on the right side and the blood is fluid The left ventricle is hard and firmly contracted if examined within a few hours after death Massive subendocardial hæmorrhages may occur (*Wilson*) The lungs show marked engorgement Various organs such as liver and kidneys show signs of congestion and hyaline degeneration The adrenal cortex may show degenerative changes Areas of patchy congestion and swelling may be present in the mucous membranes of the stomach and intestines Petechial hæmorrhages in the skin and mucous membranes may occur in severe cases

Blood Chemistry A diminution of blood chlorides and plasma bicarbonates and increase of blood lactic acid are the usual findings An increase of blood urea and sugar is occasionally seen

CLINICAL TYPES

HYPERPYREXIAL TYPE *Vide infra*

GASTRIC TYPE It is characterised by normal axillary but high rectal temperature and marked gastro intestinal disturbances such as epigastric pain and vomiting The liver is enlarged and the knee-jerks are absent Death may occur in 4-10 days from hyperpyrexia

CHOLERAIC TYPE It is characterised by sudden onset with the passage of frequent watery stools associated with vomiting *The temperature varies from 100° 102°F The picture resembles cholera* Death may occur within 3-4 days

CLINICAL MANIFESTATIONS

MODE OF ONSET The onset may be sudden but more commonly gradual In the first group the patient rapidly develops high fever

It should be remembered however that malaria often co-exists with heat hyperpyrexia in the tropics

CEREBROSPINAL MENINGITIS 1 Characteristic lateral decubitus with head retraction and Kernig's sign 2 Presence of herpes labialis 3 Presence of leucocytosis 4 Characteristic spinal fluid changes

CEREBRAL HÆMORRHAGE 1 Occurrence of high fever which follows the loss of consciousness 2 Presence of paralytic manifestation 3 Presence of blood in the spinal fluid on lumbar puncture

URÆMIA 1 Absence of high fever 2 Presence of the characteristic urinary finding such as albumin granular and epithelial casts 3 Appreciable increase in the urea and non protein nitrogen contents of the blood

OPIUM POISONING 1 History of taking opium 2 Cold clammy skin 3 Cyanosis

DIABETIC COMA 1 Sugar and acetone in urine 2 High blood sugar

GENERAL MANAGEMENT

DIET If the patient is unconscious oral feeding is not practicable Nasal feeding and nutrient rectal enemata are necessary

CONVALESCENCE Prolonged rest in a cool and quiet room is necessary till the convalescence is well established Return to work should be very gradual A change to a cooler climate is very helpful A regular action of the bowels should be maintained by mild laxatives such as liquid paraffin or cascara The diet should be adequate in calories and vitamins and balanced regarding the various constituents No alcohol should be allowed

SPECIFIC TREATMENT

As hyperpyrexia is due to failure of sweating the aim is to reduce temperature and promote sweating Patient is to be put in a dark quiet and cool room An air conditioned room is ideal The clothes are removed from the body The patient is then wrapped in a wet sheet or covered with thin cloth and sprayed with cold or iced water and fanned vigorously Constant air circulation is essential We would emphasize here that too much application of ice to the skin constricts the cutaneous capillaries and retards heat loss by evaporation (*Hill*) Repeated attempts at reduction of the rectal temperature down to 102°F are made by resorting to various measures of hydro-

SEQUELÆ

1 Myocardial weakness It may persist for days or weeks 2 Relapses Liability to relapse is present until weeks have passed after the return of temperature to normal 3 A low continued pyrexia It may persist for about 3 weeks 4 Persistent headache 5 Persistence of cerebral or cerebellar symptoms for month probably due to organic damage 6 Psychoses Dementia in 10 per cent of severe cases and suicide in 5 per cent (*Rogers*)

PROGNOSIS

It is influenced by the following factors

AGE Mortality is high in persons over 40 years

CO EXISTENCE OF OTHER DISEASES such as malaria typhoid fever dengue cardiac renal or pulmonary diseases and diabetes mellitus are of bad prognostic significance Debilitating conditions render the prognosis unfavourable

CLINICAL CONDITION The prognosis is very grave in the choleraic type and in absence of knee jerks The mortality rate rises with a temperature of 107°F or more

TREATMENT A delay in treatment for more than 3 hours after the occurrence of coma is invariably fatal

DIAGNOSIS

A diagnosis of heat hyperpyrexia may be easily made from a consideration of the following data

1 Presence of predisposing atmospheric conditions such as high air temperature and relative humidity associated with lack of air movement

2 History of exposure to sun or high temperature for a long time

3 Presence of hot dry skin with a high body temperature above 106°F

4 If urinary output of chloride falls below 3 g in 24 hours the condition is suggestive of heat hyperpyrexia

DIFFERENTIAL DIAGNOSIS

Heat hyperpyrexia should be differentiated from the following

CEREBRAL MALARIA 1 Presence of rigors 2 Presence of icteric tinge of the conjunctivæ 3 Presence of an enlarged spleen 4 Presence of malaria parasites in the peripheral blood

It should be remembered however that malaria often co exists with heat hyperpyrexia in the tropics

CEREBROSPINAL MENINGITIS 1 Characteristic lateral decubitus with head retraction and Kernig s sign 2 Presence of herpes labialis 3 Presence of leucocytosis 4 Characteristic spinal fluid changes

CEREBRAL HEMORRHAGE 1 Occurrence of high fever which follows the loss of consciousness 2 Presence of paralytic manifestations 3 Presence of blood in the spinal fluid on lumbar puncture

URÆMIA 1 Absence of high fever 2 Presence of the characteristic urinary findings such as albumin granular and epithelial casts 3 Appreciable increase in the urea and non protein nitrogen contents of the blood

OPIUM POISONING 1 History of taking opium 2 Cold clammy skin 3 Cyanosis

DIABETIC COMA 1 Sugar and acetone in urine 2 High blood sugar

GENERAL MANAGEMENT

DIET If the patient is unconscious oral feeding is not practicable Nasal feeding and nutrient rectal enemata are necessary

CONVALESCENCE Prolonged rest in a cool and quiet room is necessary till the convalescence is well established Return to work should be very gradual A change to a cooler climate is very helpful A regular action of the bowels should be maintained by mild laxatives such as liquid paraffin or cascara The diet should be adequate in calories and vitamins and balanced regarding the various constituents No alcohol should be allowed

SPECIFIC TREATMENT

As hyperpyrexia is due to failure of sweating the aim is to reduce temperature and promote sweating Patient is to be put in a dark quiet and cool room An air conditioned room is ideal The clothes are removed from the body The patient is then wrapped in a wet sheet or covered with thin cloth and sprayed with cold or iced water and fanned vigorously Constant air circulation is essential We would emphasize here that too much application of ice to the skin constricts the cutaneous capillaries and retards heat loss by evaporation (*Hill*) Repeated attempts at reduction of the rectal temperature down to 102°F are made by resorting to various measures of hydro

therapy such as (1) *ice cradling* (2) *iced enemata* (3) *cold packs* (4) *immersion in cold bath* at 65°F for 20 30 minutes supplemented with a vigorous massage of the limbs to maintain the peripheral circulation

SYMPTOMATIC TREATMENT

CIRCULATORY FAILURE *Administration of suitable circulatory* stimulants Care should be taken to avoid the use of strychnine for fear of producing convulsions

RESPIRATORY FAILURE 1 Artificial respiration continued for an hour or more 2 Inhalation of oxygen bubbled through warm water at the rate of 300 500 bubbles per minute by nasal catheter The use of a tent is preferable

CONVULSIONS 1 Hypodermic injections of sodium luminal gr 3 dissolved in 1 c cm of distilled water 2 Intramuscular injection of paraldehyde 10 12 c cm 3 Inhalation of chloroform 4 Rectal enema containing chloral hydrate and potassium bromide in doses of 20 grains each

COMA 1 Lumbar puncture to relieve the raised intracranial tension is of great value 2 Rectal administration by the drip method of ice cold water containing sodium chloride gr 120 and sodium bicarbonate gr 60 to the pint It is helpful in combating hypochloræmia acidosis and hyperpyrexia 3 Intravenous administration of 50 100 c cm of 25 50 per cent glucose or sucrose solution

PREVENTIVE MEASURES

During spell of high atmospheric temperature and humidity especially with a wet bulb temperature above 80°F the following measures should be adopted

1 Protection of the head by fibre glass hat and umbrellas 2 *Wearing light and loose clothes of white fabric* 3 Avoidance of strenuous exercises 4 Maintenance of adequate fluid and salt intake (about 10 20 g of sodium chloride a day) 5 Avoidance of alcohol 6 Use of electric and hand fans to promote air movements 7 Closing of the windows and shutters during the noon to prevent the entrance of hot air 8 Construction of well ventilated houses with thick walls and roofs to prevent heating by the rays of the sun 9 Provision of air conditioned rooms or buildings wherever practicable

Heat Exhaustion

[Heat collapse Heat shock Heat prostration]

DEFINITION

It is a clinical condition characterised by signs and symptoms of peripheral failure as a result of exposure to heat

ÆTIOLOGY

It is a minor form of heat hyperpyrexia People working in the engin rooms and stoke holds are especially liable Heat exhaustion may occur in debilitated and elderly persons with a low cardiac reserve during the hot weather even in the temperate climat The syndrome is characterised by some inhibition of sweating

CLINICAL MANIFESTATIONS

Symptoms appear during exposure to heat or a few days later The patient complains of weakness headache giddiness faintness anorexia nausea and occasionally vomiting There is always a history of extensive and recurrent prickly heat The face is pale the pulse weak and rapid pupil dilated and respirations rapid and shallow The bloodpressure falls markedly as a result of the peripheral vasodilatation The temperature is variable It is usually subnormal but occasionally moderately high (101 103°F) Patient may be conscious semi conscious or rarely comatose Rapid recovery usually occurs with prompt and early treatment In late cases and in person over 60 years with a low cardiac reserve death may occur from syncope and hyperpyrexia

COMPLICATIONS

1 Syncopal failure 2 Hyperpyrexia

DIAGNOSIS

It is made by the following data

1 Predisposing climatic conditions 2 Sudden onset of circulatory collapse

PROGNOSIS

The prognosis is better than in heat hyperpyrexia Recovery takes place rapidly Headache and slight weakness may persist for a few hour

TREATMENT

It consists in the adoption of general measures such as removal of the patient from the heat to a cool airy shaded place and ensuring

rest in bed Adoption of the following symptomatic measures to avoid peripheral failure 1 Rest in bed with foot end raised about a foot above the floor 2 Hydrotherapeutic measures to lower the high internal temperature if there be any 3 Use of circulatory stimulant

In mild cases (*a*) inhalation of ammonia (*b*) oral administration of half a drachm each of aromatic spirits of ammonia and ether

In moderately severe cases (*a*) nor adrenaline drip intravenously in 5 per cent glucose dissolved in normal saline (*b*) 2 c cm of niketha mide intramuscularly (*c*) 20 mg pholedrine intramuscularly

4 Administration of normal or hypertonic saline by the intra venous route or of normal saline with 2 per cent sodium bicarbonate by the rectal drip method

PREVENTIVE MEASURES

Same as in heat hyperpyrexia

Heat Cramps

[Miner s cramps Fireman cramp Stoker s cramps]

DEFINITION

It is also a minor form of heat effect due to muscular exertion in a hot moist atmosphere characterised by tetany of the voluntary muscles due to loss of salts and water through excessive sweating

ETIOLOGY

It is the same as described under heat hyperpyrexia except that co existing diseases such as malaria typhoid fever etc play little or no part in its causation Persons working in the mines and stoke holds where the atmosphere is hot and moist are especially affected

CLINICAL MANIFESTATIONS

The onset may be heralded by prodromata such as headache giddiness nausea diarrhœa and muscular twitchings Then the patient complains of severe painful cramps affecting chiefly the calves arms and occasionally the abdominal muscles which are felt as hard as metal bars during the stage of contraction Marked sweating precedes and occurs during the cramps Soreness is present in the affected muscles for a day or two The blood shows a high specific gravity relative polycythæmia with raised hæmoglobin value slight leucocytosis an increase of plasma protein

and a diminution of chlorides due to excessive loss of fluid and salts through sweating

TREATMENT

The main object of treatment is to replace as quickly as possible the lost water and chlorides of the body after the patient has been removed to a cool place For this purpose administration of a pint of normal saline by the intravenous route or by the rectal drip method is very helpful In mild cases rest in bed with saline drink of the strength described under preventive measures of heat hyperpyrexia is all that is required to relieve the distressing symptoms

PREVENTIVE MEASURES

Drinking of adequate quantities of water with the addition of sodium chloride gr 10 to the pint during the heat waves is an effective preventive measure

J C B

rest in bed Adoption of the following symptomatic measures to avoid peripheral failure 1 Rest in bed with foot end raised about a foot above the floor 2 Hydrotherapeutic measures to lower the high internal temperature if there be any 3 Use of circulatory stimulants

In mild cases (a) inhalation of ammonia (b) oral administration of half a drachm each of aromatic spirits of ammonia and ether

In moderately severe cases (a) nor adrenaline drip intravenously in 5 per cent glucose dissolved in normal saline (b) 2 c.cm of niketha mide intramuscularly (c) 20 mg pholedrine intramuscularly

4 Administration of normal or hypertonic saline by the intra venous route or of normal saline with 2 per cent sodium bicarbonate by the rectal drip method

PREVENTIVE MEASURES

Same as in heat hyperpyrexia

Heat Cramps

[Miners cramps Firemans cramps Stokers cramps]

DEFINITION

It is also a minor form of heat effect due to muscular exertion in a hot moist atmosphere characterised by tetany of the voluntary muscles due to loss of salts and water through excessive sweating

ETIOLOGY

It is the same as described under heat hyperpyrexia except that co existing diseases such as malaria typhoid fever etc play little or no part in its causation Persons working in the mines and stoke hold where the atmosphere is hot and moist are especially affected

CLINICAL MANIFESTATIONS

The onset may be heralded by prodromata such as headache, giddiness, nausea diarrhœa and muscular twitchings Then the patient complains of severe painful cramps affecting chiefly the calves arms and occasionally the abdominal muscles which are felt as hard as metal bars during the stage of contraction Marked sweating precedes and occurs during the cramps Soreness is present in the affected muscles for a day or two The blood shows a high specific gravity relative polycythæmia with raised hæmoglobin value slight leucocytosis an increase of plasma protein

PREDISPOSING FACTORS Heredity habits and occupation do not appear to play any significant role Family susceptibility has been reported by a few workers Allergic diatheses is obtainable in some cases

THEORIES OF CAUSATION There is no single ætiological agent that could be incriminated as the sole cause Two theories one of allergy and the other of infection have been advanced to explain the various manifestations of the disease

Theory of Allergy The presence of increased number of eosinophils in blood bone marrow and sputum bronchial spasm with lung infiltrations history of other allergic manifestations and favourable response to ACTH cortisone or allied drugs suggest that the various manifestations of the disease may represent allergic responses to some antigen The exact nature of the allergen however remains obscure It has variously been ascribed to the sensitising effect of ascaris (*Loeffler*) strongyloides nematodes microfilariæ trichinia mites (*Carter et al*) and the various bacterial flora in the upper respiratory tract or in nasal sinuses It is possible that the various agents enumerated will sometime produce a condition like tropical eosinophilia either directly or indirectly through the sensitisation mechanism These agents singly or in combination could however be isolated only from a few cases Thorough investigations in the majority of cases provide no substantial proof in favour of the parasitic or bacterial organisms acting directly or as allergens Multiplicity of agents implicated is also an argument against their specific role as causal agents

Theory of Infection Characteristic course of the disease with occasional fever simultaneous incidence in more than one member of the family leucocytosis enlargement of lymphnodes and spleen (in some cases lymphadenopathy and splenomegaly may also be seen in allergic conditions) serological findings the presence of cold hæmagglutinins and positive W I (in some cases) raised erythrocyte sedimentation rate response to arsenic and aureomycin all together go to favour an infective origin The infective agent is however yet to be identified Following agents have been incriminated from time to time

(*a*) *Mit* Carter Wedd and D Abrera working in Ceylon detected mites of the genera *Tarsonemus* in the sputum of some cases of tropical eosinophilia Following arsenic therapy the mites were absent or grossly macerated Carter and D Abrera introduced mite eggs into the trachea of a monkey which manifested eosinophilia and

SECTION X DISEASES OF UNKNOWN ÆTIOLOGY

CHAPTER I

TROPICAL EOSINOPHILIA

DEFINITION

A syndrome with high eosinophilia characterised by loss of weight low grade fever and cough clinically resembling bronchial asthma or pulmonary tuberculosis with characteristic radiographic changes in the lungs

HISTORY

Roy and Basu (1918) from Calcutta were the first to recognise the syndrome now known as tropical eosinophilia Later Loeffler (1932) in Switzerland described a syndrome in which eosinophilia was associated with transient pulmonary infiltrations Frimodt Moller and Barton (1940) working in India described in details the clinical features blood picture and radiographic appearances of a large group of patients and clearly differentiated the condition from pulmonary tuberculosis Three years later Weingarten (1943) in India gave a comprehensive account of the syndrome under the tittle of tropical eosinophilia Since then numerous case reports have been published under different names but generally confirming the previous findings

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION The disease occurs most commonly in India and Ceylon It has also been reported from Burma Thailand Malaya the East Indies China tropical Africa northern part of South America and the West Indies A few cases have been reported from Korea and Australia Weingarten thought that the disease was confined to the coastal districts of India Recent reports indicate that the disease is widely prevalent all over India Humidity of the atmosphere may be a predisposing factor

SEASONAL PREVALENCE There is no definite seasonal incidence The symptoms may however exacerbate during the rains or in winter

AGE AND SEX INCIDENCE The disease has been observed in all ages The peak incidence in most regions is found in the age group 20 40 years There is no especial predilection to any particular sex

CLINICAL TYPES

1 ACUTE TYPE This is the less common type There is sudden onset of high fever with unproductive cough chest pain and hurried respiration The picture in general resembles that of acute bronchiolitis and there may be similar pulmonary signs Loss of appetite and weight may follow within a few days Skiagram of chest shows disseminated mottlings distributed uniformly throughout the lung fields These acute cases in their natural course may remit spontaneously within a few days or more commonly pass into the chronic type

2 CHRONIC TYPE This is by far the commoner type The illness begins insidiously with lassitude loss of appetite and weight mild fever and cough The cough is usually dry hacking in character paroxysmal in nature and worse at night There is little cough during the day In the early stage sputum if there is any is scanty viscid and brought up with difficulty At first the paroxysms are mild and brief later these increase in severity and duration Paroxysms may last from a few minutes to half an hour often repeating several times during the same night The patient is forced to sit up and his sleep is badly disturbed Following a paroxysm of cough there is varying degree of dyspnoea and frequently a feeling of suffocation along with hurried and panting respiration Respiratory distress may resemble that of asthma but bronchial spasm is not always present and the dyspnoea is not always expiratory Some patients may however show true bronchospasm

CLINICAL MANIFESTATIONS

MODE OF ONSET The onset is usually insidious The common symptomatology in an average case includes (i) cough worse at night often paroxysmal in nature with mucoid or mucopurulent sputum and sometimes blood (ii) dyspnoea (iii) mild fever (iv) progressive loss of weight and (v) insomnia

RESPIRATORY SYSTEM During a severe paroxysm physical signs in the chest are those of bronchial asthma In less severe cases scattered sibilant or sonorous rhonchi may be heard over both the lung There may be coarse basal rales Adventitious sounds are rarely heard in the apices The expiration is prolonged Signs of emphysema are common In about 20 per cent of cases there may be no obvious physical signs Many patients complain of a sense of constriction in the chest during and for sometime after a paroxysm of cough There may be a dull aching pain over the front of the chest which probably

symptomatology simulating the human disease It has been suggested that mites might act as vectors of some still unidentified causative organism Many subsequent workers failed to detect mite and in general mite theory is not acceptable

(*b*) *Bacteria* Frimodt Moller suggested a tuberculous ætiology of the condition Shircore reported the finding of a small spirochete in the sputum Bacterial theory cannot be supported in the ab ence of any specific organism that can be consistently demonstrated

(*c*) *Virus* On the analogy of primary atypical pneumonia and infectious mononucleosis it has been suggested that the condition might be a viral infection Transient serological reactions (positive W R and presence of cold hæmagglutinins) response to aureomycin and the production of an analogous disease in experimental animals by the injection of Seitz filtered serum from patients with tropical eosinophilia (*Misra et al*) point to a viral ætiology which can only be established when the still elusive virus has been isolated and characterised

(*d*) It has been suggested that the disorder may be an atypical manifestion of infection with nematode or some form of non human filarial parasite

PATHOLOGY

Autopsy report (*Viswanathan*) from a patient who died of arsenical encephalopathy provides the basis of pathological changes recorded here Histological section of the lungs revealed scattered and discrete areas of interstitial fibroblastic proliferation and eosinophilic infiltration with some of the adjacent alveoli partially or completely filled with macrophages These areas of partial consolidation were in close relation to the terminal bronchioles In a few areas nodular structures made up of monocytes were pre ent Based on the histological changes it was assumed that the infection in tropical eosinophilia was acquired probably by inhalation The infecting agent invades the peribronchial tissue and sets up an inflammatory process involving the interstitial tissue mainly and alveoli partially

In the earlier stage the cellular infiltrations monocytic and eosinophilic appear in discrete or scattered fashion Later in the chronic stage are seen the nodules made up of giant cells and monocytes The radiographic appearance of disseminated mottlings in pulmonary parenchyma represents in all probability the cellular infiltrations described above

tuberculosis but are not so dense well circumscribed and diffusely disseminated Very fine mottling sometimes give rise to a peculiar misty appearance

In the long standing cases there may be patchy basal emphysema and accentuation of the pulmonary conus of the heart shadow

The radiological patterns do not usually follow any definite order of evolution The extent of the radiological signs cannot always be correlated with the clinical and hæmatological picture The shadows however disappear quickly with therapy

COMPLICATIONS

STATUS ASTHMATICUS It may develop in an occasional case

PROGNOSIS

The symptoms usually develop gradually and it may be weeks or months before the full blown picture is established The disease tends to be chronic and may last for years with alternate periods of remission and exacerbation The disease is not fatal and in general runs a fairly benign course Spontaneous recovery may occur after a varying period often after some acute bacterial infection Response to treatment is usually prompt and remarkable Relapses and recurrences however occur in a small proportion of cases when therapy is still equally effective

DIAGNOSIS

CLINICAL DATA. The condition should be suspected when there are symptoms of weakness wasting and cough with or without pulmonary signs suggestive of bronchitis asthma or pulmonary tuberculosi

LABORATORY DATA Blood count confirms the diagnosis the total number of eosinophils should exceed 3 000 per c mm of blood In an average case higher values of eosinophils are obtained Eosinophilic counts between 2000-3000 per c mm of blood is suspicious and should be followed up

DIFFERENTIAL DIAGNOSIS

PULMONARY TUBERCULOSIS The lung signs and x ray appearances may be confused with pulmonary tuberculosis Points of distinction are the presence of (1) apical and subapical crepitations in tuberculosis (in eosinophilia the lesions are mostly basal apices being usually free) (2) sputum test for acid fast bacilli positive and (3) favourable response with anti tuberculous drugs

results from overaction of the accessory muscles of respiration Epigastric pain may also be present during and after a bout of cough and sweating frequently accompanies and follows a paroxysm After a bout of cough there may be mucoid or mucopurulent expectoration of varying degree The sputum sometime contains streaks of blood and small hæmoptyses may occur in a few cases

LYMPHATIC SYSTEM In some cases slight enlargement of spleen and/or enlargement of one or more groups of lymphnodes are seen Incidence of lymphadenopathy appears to be higher in children

CIRCULATORY SYSTEM Usually there are no circulatory disturbances Heart is not dilated The pulse may be rapid during the paroxysms of cough and respiratory distress but is otherwise normal

BLOOD Eosinophilic leucocytosis is characteristic Common values for total white cells are 15 000 to 30 000 per c mm of which eosinophils may constitute 25 to 90 per cent Cases are on record where total eosinophil count was as high as 100 000 per c mm Counts may fluctuate widely without any apparent cause Occasional eosinophilic myelocyte or metamyelocyte may be seen Intercurrent infection tends to reduce the eosinophil count which may again rise after the infection has subsided P B C and hæmoglobin levels are usually within normal limits E S R is raised in most of the cases

BONE MARROW Erythropoiesis is always normoblastic Mature orthochromatic normoblasts constitute the major bulk of normoblasts All forms of eosinophils from myelocyte to granulocyte are increased A number of eosinophils particularly the mature forms show cytoplasmic vacuolation Neutrophils are relatively depressed Lymphopoiesis and thrombocytopoiesis show no significant change (*Das Gupta and Chatterjea*)

SEROLOGY Significant titre of cold agglutinins as reported by Viswanathan and Natarajan may be found only rarely W R may be positive in approximately 30 per cent of cases

RADIOLOGICAL FINDINGS The three characteristic features are (*i*) increase of normal striations (*ii*) miliary mottlings and (*iii*) exaggerated hilar shadows which occur sometimes singly but more commonly in combination Mottling is present in most cases at some stage or other Mottlings which may be fine or course are polymorphic in character and appear as soft rounded ill defined spots of varying size (from pin head to 3 cm across) They are most prominent in the bases and midzones The shadows resemble those of pulmonary miliary

tuberculosis but are not so dense well circumscribed and diffu ely disseminated Very fine mottling sometimes give rise to a peculiar misty appearance

In the long standing cases there may be patchy basal emphysema and accentuation of the pulmonary conus of the heart shadow

The radiological patterns do not usually follow any definite order of evolution The extent of the radiological signs cannot always be correlated with the clinical and hæmatological picture The shadows however disappear quickly with therapy

COMPLICATIONS

STATUS ASTHMATICUS It may develop in an oc a ional case

PROGNOSIS

The symptoms usually develop gradually and it may be weeks or months before the full blown picture is established The disease tends to be chronic and may last for years with alternate periods of remission and exacerbation The disease is not fatal and in general runs a fairly benign course Spontaneous recovery may occur after a varying period often after some acute bacterial infection Response to treat ment is usually prompt and remarkable Relapses and recurrences however occur in a small proportion of cases when therapy is still equally effe tive

DIAGNOSIS

CLINICAL DATA The condition should be suspected when there are symptoms of weakness wasting and cough with or without pulmonary signs suggestive of bronchitis asthma or pulmonary tuberculosis

LABORATORY DATA Blood count confirms the diagno is the total number of eosinophils should exceed 3 000 per c mm of blood In an average case higher values of eosinophils are obtained Eosinophilic counts between 2000 3000 per c mm of blood is suspicious and hould be followed up

DIFFERENTIAL DIAGNOSIS

PULMONARY TUBERCULOSIS The lung signs and x ray appear ances may be confused with pulmonary tuberculosis Points of di tinction are the presence of (1) apical and subapical crepitations in tuberculo is (in eosinophilia the lesions are mostly basal apices being usually free) (2) sputum test for acid fast bacilli po itive and (3) favourable re ponse with anti tuberculou drugs

Asthma with chronic bronchitis is similarly differentiated

PARASITIC INFECTIONS AND SKIN AFFECTIONS The eosinophilia is usually of lower order (within 2 000) the finding of parasites and their eradication with specific drugs serve to differentiate these condition

HODGKIN S DISEASE OR EOSINOPHILIC LEUKÆMIAS are differentiated by the clinical history the enlargement of spleen and lymphnodes and the examination of bone marrow and lymphnode by biopsy

LOEFFLER S SYNDROME In this condition the eosinophil count is very high but the total white cell count is relatively low The lung changes are transitory and clear up spontaneously in an average case within a week

GENERAL MANAGEMENT

Rest should be enforced during the febrile period and the earlier part of the arsenic therapy For distressing cough sedative and anti spasmodics may be prescribed Penicillin is useful in cases associated with secondary infections

SPECIFIC TREATMENT

PIPERAZINE At present *diethylcarbamazine* is the drug of choice

Dose is 12 mg per kg body weight per day by mouth Adult patient in average would require 12 16 tablets (50 mg each tablet) daily for 7 10 days The symptoms are usually relieved in about a week s time and the eosinophilic count falls almost to a normal level in 2 5 weeks time Relapses also respond to the drug

ANTIBIOTIC *Aureomycin* 1 g daily (250 mg each capsule) for 10 days Clinical and hæmatological improvement ensues in some ca es Two courses may be required to bring about the desired effect The results on the whole are unpredictable and the drug is therefore not recommended for routine use

ARSENIC Most of the cases also respond readily to a course of organic arsenicals given parenterally Results by the oral route are unsatisfactory After 1 to 2 injections eosinophils in the peripheral blood may increase temporarily which in a few cases may be associated with exacerbation of symptoms Treatment continued thereafter brings about rapid clinical and hæmatological improvement In an average case blood picture becomes normal in 4-6 weeks The radiological signs disappear fairly quickly along with clinical and hæmatological improvement

Relapses with return of clinical signs blood eosinophilia and radiological pattern may occur after a full course of arsenic therapy in approximately 20 per cent of cases Relapses usually ensue within two years A further course of arsenic will control the relapse

Acetylarsan 2 to 3 c cm intramuscularly at an interval of 3 to 5 days *till 6 to 9 injections are given It is better to start with smaller* doses at the beginning to avoid toxic reactions

No arsenobillon or *Mapharside* 0 30 to 0 45 g intravenously at an interval of 4 to 6 days till 6 to 9 injections are given

Carbarsone 0 25 g tablets or pulvules orally given twice daily after meals for 7 to 10 days All the usual precautions should be taken during arsenic therapy

In view of the possible toxic reactions treatment with arsenic can no longer be recommended for routine use It may be given only when there has been no response to *diethylcarbamazine*

STEROID HORMONES In usual therapeutic dosage these hormones effect rapid improvement in clinical and hæmatological picture The effect is however transitory the usual signs and symptoms recurring shortly after withdrawal of the drugs

ACTH is usually given intramuscularly in the dosage of 40 to 100 mg daily in two divided doses for a period of two to three weeks

Cortisone is usually given orally 100 to 200 mg daily distributed in four six hourly doses for a similar period

Prednisone or prednisolone tablets in 20 mg daily dose is ordinarily preferable to ACTH or cortisone

These hormones do not have any place in the routine management of tropical eosinophilia They are indicated in status asthmaticus and in refractory cases

J B C

CHAPTER II

TROPICAL SPLENOMEGALY

[Bengal splenomegaly (D) Splenomegaly of unknown etiology]

DEFINITION

It is a very chronic disease of unknown etiology characterised by primary splenomegaly varying degrees of anaemia and terminal hepatic cirrhosis

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION It is common in W Bengal occurring mostly in western and south western parts of the province In W Bengal it occurs mostly in rural and occasionally in urban areas Cases also occur in other parts of India and E Pakistan

AGE AND SEX INCIDENCE Young adults are mostly affected Children and old people are rarely affected It is commoner in males

THEORIES OF CAUSATION

The exact cause of the malady is not known The following theories have been advanced

MALARIAL THEORY The malady is probably a manifestation of hypersensitive cellular reaction occurring in partially immune population in response to malarial infection Febrile attacks occurring early in the disease and responding to antimalarial treatment support this theory

Chaudhuri and his associates have shown that the majority of cases as seen in W Bengal result from chronic latent malarial infection malnutrition being an associated factor Hepatic damage and signs of portal obstruction are traceable to these factors

DE'S THEORY De showed that the disease in question was entirely distinct from malaria and kala azar He suggested that the disease was probably the result of An infective element of low virulence working for a very long time and producing a toxic material causing necrosis and ultimately cirrhosis of the liver and spleen But the infective element has not been demonstrated

PATHOLOGY

Pathological features as described by De are given below

SPLEEN It is uniformly enlarged and hard The histological picture of the spleen is very characteristic In a typical case the

normal structure of the spleen is distorted with loss of splenic pattern The capsule becomes thickened with numerous and prominent trabeculæ and evidences of perisplenitis The malpighian follicles undergo almost complete atrophy The splenic sinuses are widely dilated and packed with lymphocytes and numerous multi nucleated giant cells containing engulfed erythrocytes and leucocytes The actual pulp tissue thus undergoes gradual pressure atrophy In very advanced cases both the reticulum and fibrous tissues are considerably increased giving a firm consistency to the organ

LIVER The liver shows dilatation of the sinusoids and fatty change in the hepatic cells particularly in advanced cases with anæmia The portal spaces show varying degrees of round cell infiltration and proliferation of fibrous tissue Advanced cases with ascites show a structure similar to portal type of cirrhosis

BONE MARROW It is hyperplastic There is active erythropoiesis with normoblastic hyperplasia Granulopoiesis is also active Megakaryocytes are normal or increased with a variable degree of activity

CLINICAL MANIFESTATIONS

MODE OF ONSET It is insidious Some of the cases start with intermittent fever closely simulating malaria The fever at first seems to subside with antimalarial treatment though malarial parasite is not found in the blood During subsequent bouts of fever antimalarial treatment is hardly effective The spleen gradually enlarges and patient complains of langour lassitude progressive weakness and gradually failing health Some of the patients may have epistaxis or hæmatemesis at this stage In an average case within 3 to 5 years the liver shows moderate enlargement with icteric tinge in the conjunctivæ In another 2 to 3 years signs of hepatic cirrhosis *e g* ascites hæmatemesis develop and frank jaundice may result

BLOOD PICTURE Varying degree of anæmia is the rule De described the usual type of anæmia as microcytic and hypochromic Slightly macrocytic anæmias are however found quite frequently In some cases the reticulocyte count is high but there is no evidence of spherocytosis The red cells in some cases are hyperresistant to hypotonic salt solutions Moderate to marked leucopenia is the rule with relative decrease of neutrophils and increase of lymphocytes Thrombocytopenia of varying degree is also a common finding

Globulin fraction of plasma is increased The formolgel test is negative while urea stibamine test may be positive in a

few cases Wassermann reaction is always negative De found urea and N P N contents of the blood moderately raised but cholesterol sugar and chlorides remain normal There is usually slight hyperbilirubinæmia the bilirubin content of the plasma usually varying from 0·6 mg to 1·8 mg per cent Routine cultural examinations of the blood splenic juice and bone marrow have always been negative for flagellates, malaria parasites and bacteria

Cytological study of bone marrow usually shows a cellular marrow with normoblastic erythropoiesis

PROGNOSIS

The disease runs a very chronic course, usually extending for 10 to 12 years. Ultimate prognosis of the disease is very unfavourable The patients succumb either to some intercurrent infection chiefly pneumonia dysentery and pulmonary tuberculosis or develop a terminal cirrhosis of the liver with ascites jaundice and hæmatemesis

DIAGNOSIS

It has no specific diagnostic sign and the diagnosis is made by a process of exclusion after considering all other forms of splenomegaly All the known tests for malaria and kala azar are negative Hæmogram and myelogram at once differentiate the condition from leukæmias The spleen is much more enlarged than in most cases of ordinary hepatic cirrhosis and splenic enlargement antedates hepatic enlargement by many years No discussion on tropical splenomegaly can be complete without reference to splenic anæmia a term which is synonymous with Banti s disease or Banti s syndrome There are many points of similarity between the two diseases In both the conditions the ætiology is obscure and the essential clinical features of primary splenomegaly anæmia and hepatic cirrhosis are similar if not identical Closer scrutiny of the two conditions however brings out certain points of difference which are shown in a tabular form

Tropical Splenomegaly	*Splenic Anæmia*
Febrile paroxysm usually common during the earlier part of the disease	Usually afebrile
Hæmorrhages less common	Hæmorrhages especially hæmatemesis commoner even before the advent of hepatic cirrhosis

Tropical Splenomegaly	*Splenic Anæmia*
Macrocytic or dimorphic blood picture quite common hypochromic blood picture in a few cases	Blood picture usually hypochromic
Pathology (i) Numerous multinucleated giant cells showing evidences of hæmatophagy are characteristically seen in widely dilated splenic sinuses	(i) Multinucleated giant cells scanty and not always seen
(ii) Fibrosiderotic nodules or Gandy Gamna bodies only rarely seen	(ii) Fibrosiderotic nodules formed by the organisation of periarteriolar hæmorrhages are characteristic features

TREATMENT

Treatment is unsatisfactory in view of the still unknown ætiology In view of the possibility of a malarial background it would be wise to start off with a schedule of prolonged suppressive antimalarial therapy, such as advocated by Chaudhuri Camoquin (0 2 g) with or without primaquin (10 mg) every fortnight for a year In addition the general treatment includes high portein diet crude liver extracts parenterally ferrous sulphate tablets orally, vitamins and repeated bloodtransfusion in resistant cases

In cases not responding to the above regimen the question of splenectomy must be reviewed Splenectomy done early in the disease before hepatic cirrhosis has supervened cures a fair number of cases It is advocated on the assumption that splenic changes, whatever may be their cause are responsible for gradual deterioration of the patient and terminal hepatic cirrhosis All the cases are not however uniformly benefited by splenectomy In view of associated portal obstruction it is desirable that splenectomy must be supplemented by various shunt operations i.e. splenorenal and portocaval In the present state of our knowledge it will be reasonable to restrict splenectomy to those cases (i) which are refractory to general hæmatinic and supportive treatment and (ii) which show recurrent relapses of anæmia and hæmorrhage Where splenectomy is not practicable ligature of splenic artery has been done by some workers but the results are not encouraging

J B C

CHAPTER III

SPRUE

[Psilosis Ceylon sore mouth Cochin China diarrhœa.]

DEFINITION

Sprue is a chronic disease of obscure ætiology associated with impairment of intestinal absorption of nutrients and characterised in a typical case by flatulent dyspepsia fatty diarrhœa sore mouth weight loss and macrocytic anæmia with megaloblastic erythropoiesis All these features may not be present in early or mild cases while variations are common at all stages of the disease Tropical sprue non tropical sprue and cœliac disease have much in common These primary conditions and allied clinical disorders secondary to organic lesions are included in a general term sprue syndrome or malabsorption syndrome

HISTORY

Sprue was described in Rome by Aristæus in ancient times and in Belgium by Ketelaer in 1669 William Hillary in Barbados reported the classical clinical picture in 1766 while Sir Patrick Manson in China and Van der Burg in Java recorded in greater details the clinical features of the disease about 1880 The term sprue was derived from the Dutch word *Sprouw* meaning aphthous stomatitis Most published clinical reports on tropical sprue dealt with the disease as seen in Europeans of long residence in the tropics Chronic watery diarrhœa with anæmia glossitis and loss of weight was long known to be prevalent in India especially among women after child birth popularly called in the Eastern part of India as *Sutika* (para sprue) Another variant of the syndrome hill diarrhœa was often reported in the past from the Himalayan hill stations and elsewhere Introduction of liver therapy has been an epoch making advance in the management of the e condition

ETIOLOGY

GEOGRAPHICAL DISTRIBUTION Predominantly a disease of the tropics and sub tropics sprue has also been reported from Europe and U S A It is said to be rare in Africa among the highly pigmented race Certain endemic areas have been recognised For instance sprue persists in Puerto Rico and Cuba but it is not observed in

Jamaica It is seen in Hong Kong but rare in Singapore In India during the World War II the diagnosis of sprue was made in a large series of military patients It occurred most (in epidemic form affecting the British and Indians as well) in Burma and Assam less in Bengal and Bombay and least in North West regions Thus within a climatic zone sprue is regional in distribution In any case the incidence of true sprue is declining

SEASONAL INCIDENCE Cases usually begin to crop up shortly after the rains and the incidence reaches its peak in November (*Rogers*) In 1943 45 the incidence of sprue in India as observed by the Armed Forces was maximum in the hot months and minimal in cold months

AGE SEX FAMILY AND RACE INCIDENCE Sprue may begin at any age but mostly after 20 years of age Both sexes are equally liable women during pregnancy being particularly susceptible Several members of the same family may be affected hence the popular name sprue houses in Ceylon The largest reported incidence of sprue is among the white people residing in the tropics but the local people are not exempted

OTHER FACTORS Prolonged residence in an endemic area and long suffering from bowel diseases like dysentery and colitis are predisposing causes While it remains possible that sprue may be initiated by a deficient diet this is not universal because the condition has often appeared in Europeans on good diet

THEORIES OF CAUSATION The real cause of sprue is yet to be established During the past two decades there have been increasing contributions on clinical biochemical pathological and therapeutic aspects of the disease

Allergy to wheat and rye glutens has been implicated as a causative factor in cœliac disease and in some cases of non tropical sprue But there is no evidence of food sensitivity giving rise to tropical sprue Abnormal metabolites arising from use of rancid fat have been incriminated but there is little evidence to support this concept Other views

Nutritional Deficiency The concept that it is predominantly a nutritional deficiency state has been widely held The remarkable clinical improvement that follows treatment with folic acid vitamin B_{12} and liver extract strongly suggests a deficiency basis But it is not

necessarily the primary cause as is borne out by the fact that sprue can occur in the well fed individuals while it may not be observed in the people thriving on marginal diet Further studies during remissions have revealed evidence of impaired intestinal absorption and clinical relapses are not uncommon despite adequate therapy to make up the suspected deficiency

Infection The chronic diarrhœa suggests the possibility of an underlying infection The specific organisms as isolated in an individual case are not however the ætiological agents although they may contribute to the bowel malabsorption defect in susceptible subjects Alteration of the bacterial flora in the bowel has been incriminated An abnormal bacterial flora in the small intestine possibly spreading from the colon may synthesize folic acid analogues interfering with cellular metabolism of intestinal mucous membrane Clinical responses of sprue to sulphaguanidine and antibiotics have been reported but they are not convincing Bacteriological studies of the jejunum contents indicate that the impaired nutritional absorption cannot be attributed to the effect of an altered bacterial flora The old view of monilial infection is untenable and the fungi are mere secondary invaders Failure to identify causative organisms and the absence of fever leucocytosis or pathological changes in the intestine are points against infection as the primary cause

Metabolic Abnormality Constitutional and inherited factors may play a role in the ætiology as suggested by the racial and familial predisposition There is possibly genetically transmitted error of metabolism affecting the enzyme system and their activities for absorption etc phosphorylation of fatty acids glycerol and sugar There is a trend to regard tropical sprue as a variant of the so called idiopathic steatorrhœa attributed to primary intestinal malabsorption defined as a complex metabolic disorder that is genetically transmitted (*Adlersberg*) The inherent defect may remain latent or become patent by such precipitating factors as infection food deficiency pregnancy allergy and/or strains and stress The malabsorption may become manifest in childhood as in cœliac disease or later in life as in tropical or non tropical sprue Perhaps cases of tropical sprue have a defect of lesser magnitude than in the other two Although it appears that the basic defect is a metabolic failure a functional rather than a mechanical failure of absorption in the small intestine of the products of fat and carbohydrate digestion as well as vitamins and minerals the genesis is far too complex

PATHOLOGY

There is extreme emaciation and muscular wasting. The tongue is smooth, red and glazed due to loss of epithelium and atrophy of filiform papillæ. The weight of organs is markedly reduced and body stores of fat are depleted. None of these is however specific of sprue.

The bone marrow in a well developed case shows megaloblastic hyperplasia. In terminal states aplasia of the bone marrow has been recorded.

Mucosal biopsies of the small intestine (by operation or Crosby's peroral intubation) reveals mucosal atrophy with blunting and flattening of villi and consequent diminution of the total absorbing surface. The surface epithelium covering the villi appear cuboidal in shape rather than columnar with nuclei of irregular shapes and position. The number of goblet cells is increased. There are increased cellular infiltrations consisting of lymphocytes, plasma cells and eosinophils in the *lamina propria*. Although it may appear that the absorptive defect results solely from these morphological changes in the intestinal villi, it is also probable that the changes are secondary to the prolonged disturbances of absorption.

A cytological study of gastric cells has revealed abnormalities of squamous and columnar cells which appear to be similar to changes associated with pernicious anæmia. These cellular changes may continue after treatment with anti anæmic factors.

CLINICAL MANIFESTATIONS

CLINICAL STAGES. Sprue has been broadly classified into three clinical stages according to severity. In the *early (first) stage* the patient complains of fatigue, flatulence and foul motions. Laboratory investigations may reveal steatorrhœa and depletion of electrolytes. After a varying interval the patient passes into the *deficiency (second)* stage resulting from prolonged bowel malabsorption. Weight loss, glossitis, stomatitis, cheilosis and hyperkeratosis become the prominent features. Iron deficiency anæmia may be manifest. As the disease progresses further *macrocytic anæmia (third stage)* develops with megaloblastic bone marrow. There is further deterioration of health with aggravation of symptoms. These stages are not clear cut and there may be overlappings with periods of remission.

MODE OF ONSET. The onset is indefinite. *Frequently there is an* initial diarrhœa or a series of such attacks recurring at intervals of months or years. In between the attacks of diarrhœa the stool may

appear normal In the more acute cases an attack of watery diarrhœa is followed by signs of sprue In others it is a subacute and chronic process Gradually the patient becomes weak and emaciated Thus the most frequent complaints are usually the triad of diarrhœa weakness and weight loss

ALIMENTARY SYSTEM Soreness of mouth is a frequent complaint Acid and spiced foods cause discomfort The tongue becomes red and inflamed and later superficial erosions develop on its dorsal surface tip and/or border Similar lesions may appear in the buccal mucosa The condition leads to excessive salivation hence the term psilosis for the disease

Small red patches vesicles with or without aphthous ulcers may develop in the mouth In chronic cases the tongue becomes denuded of epithelium and devoid of papillæ presenting a red smooth and glazed appearance with fissures resembling raw beef Sometimes the lesions may involve the œsophagus and cause discomfort or dysphagia Secondary deficiencies of vitamin B group give rise to other change in the mouth Abdominal distension flatulence with borborygmi especially towards the evening are often complained of The appetite may be impaired Spontaneous remissions and recurrences of symptoms are apt to occur

The abdomen may have a doughy feel and the coils of the intestine may be descernible through the thin abdominal wall The abdominal distension is often out of proportion to the amount of tympany Apparently it is due to dilated loops of intestine containing both gas and liquid Usually there is no pain or tenderness The liver dullness is diminished and spleen is not palpable

Stools The patient has frequently an early morning painless diarrhœa the number of stools being one or more Usually the patient is free from diarrhœa the rest of the day but sometimes after a meal the abdomen is distended the intestines gargle and a large liquid stool with much gas is passed with a sense of relief The stools are at first watery Later when chronic they are no longer watery but are pale pasty bulky foul and frothy Ordinarily the fæces contains neither mucus nor blood

The stools are bulky due to an impaired absorption of nutrients the characteristic feature being steatorrhœa in a typical case In most cases of sprue the total fat content is over 25 per cent of the dry weight instead of normal 10 25 per cent Splitting of fat is normal and the pancreatic digestion is unimpaired The ratio of neutral fat to split

fat is 1 3 or 5 instead of normal 1 2 The pale colour of the stool is due to the formation of colourless leucobilin from stercobilin by the action of intestinal bacteria and not due to any defective secretion of bile The average daily excretion of fat exceeds 6 g The quantity of fæcal nitrogen is often raised specially during diarrhœa There is increased excretion of potassium in the stool The frothy stool are attributed to sugar fermentation and are possibly produced by combination of free fatty acids and carbonates with liberation of carbon dioxide

Microscopical examination of the stool shows plenty of fatty acid crystals yeasts and bacteria Mucus pus cells red cells and pathogenic organisms are absent in uncomplicated cases

URINARY SYSTEM Nocturnal polyuria may occur due perhaps to prolonged retention of a large volume of water in the gut Urobilin and urobilinogen may be increased in patients with anæmia Chloride is reduced in dehydrated subject

NERVOUS SYSTEM Cord changes have been reported but the finding is very rare Paræsthesia in the form of numbness or tingling may be complained of Tetany may occasionally occur in an advanced case

SKIN The patient may have a dusky or muddy complexion Patchy pigmentation may appear over the malar regions forehead and buttocks There may be follicular hyperkeratosis The nails tend to be brittle and ridged Clubbing of fingers may be present

HÆMOPOIETIC SYSTEM Anæmia is not apparent until the disease has progressed for several months In early phases anæmia is slight and the red cells are normal or slightly smaller than normal with or without evidence of hypochromia In a full blown form there is frank macrocytosis though colour index is not always increased due to associated iron deficiency Red cells may show marked variation in shape and size with the appearance of a few polychromic stippled and nucleated red cells In untreated cases the reticulocyte count is within normal limits varying from 0 4 to 2 per cent Occasionally blood smear may show megaloblasts and/or macropolycytes The white cells are reduced in number with evidence of neutropenia and relative lymphocytosis Platelets may be decreased to a variable extent Hypoprothrombinæmia may result from impaired absorption of vitamin K

Other characteristics are low bloodpressure fast pulse and reduced

appear normal. In the more acute cases an attack of watery diarrhoea is followed by signs of sprue. In others it is a subacute and chronic process. Gradually the patient becomes weak and emaciated. Thus the most frequent complaints are usually the triad of diarrhoea, weakness and weight loss.

ALIMENTARY SYSTEM. Soreness of mouth is a frequent complaint. Acid and spiced food cause discomfort. The tongue becomes red and inflamed and later superficial erosions develop on its dorsal surface, tip and/or border. Similar lesions may appear in the buccal mucosa. The condition leads to excessive salivation, hence the term psilosis for the disease.

Small red patches, vesicles with or without aphthous ulcers may develop in the mouth. In chronic cases the tongue becomes denuded of epithelium and devoid of papillæ, presenting a red, smooth and glazed appearance with fissures resembling raw beef. Sometimes the lesion may involve the œsophagus and cause discomfort or dysphagia. Secondary deficiencies of vitamin B_2 group give rise to other changes in the mouth. Abdominal distension, flatulence with borborygmi especially towards the evening are often complained of. The appetite may be impaired. Spontaneous remissions and recurrences of symptoms are apt to occur.

The abdomen may have a doughy feel and the coils of the intestine may be discernible through the thin abdominal wall. The abdominal distension is often out of proportion to the amount of tympany. Apparently it is due to dilated loops of intestine containing both gas and liquid. Usually there is no pain or tenderness. The liver dullness is diminished and spleen is not palpable.

Stools. The patient has frequently an early morning painless diarrhoea, the number of stools being one or more. Usually the patient is free from diarrhoea the rest of the day but sometimes after a meal the abdomen is distended, the intestines gurgle and a large liquid stool with much gas is passed with a sense of relief. The stools are at first watery. Later when chronic they are no longer watery but are pale, pasty, bulky, foul and frothy. Ordinarily the fæces contains neither mucus nor blood.

The stools are bulky due to an impaired absorption of nutrients, the characteristic feature being steatorrhoea in a typical case. In most cases of sprue the total fat content is over 25 per cent of the dry weight instead of normal 10-25 per cent. Splitting of fat is normal and the pancreatic digestion is unimpaired. The ratio of neutral fat to split

fat is 1 3 or 5 instead of normal 1 2 The pale colour of the stool is due to the formation of colourless leucobilin from stercobilin by the action of intestinal bacteria and not due to any defective secretion of bile The average daily excretion of fat exceeds 6 g The quantity of fecal nitrogen is often raised specially during diarrhœa There is increased excretion of potassium in the stool The frothy stools are attributed to sugar fermentation and are possibly produced by combination of free fatty acids and carbonates with liberation of carbon dioxide

Microscopical examination of the stool shows plenty of fatty acid crystals yeasts and bacteria Mucus pus cells red cells and pathogenic organisms are absent in uncomplicated cases

URINARY SYSTEM Nocturnal polyuria may occur due perhaps to prolonged retention of a large volume of water in the gut Urobilin and urobilinogen may be increased in patients with anæmia Chloride is reduced in dehydrated subjects

NERVOUS SYSTEM Cord changes have been reported but this finding is very rare Paræsthesia in the form of numbness or tinglings may be complained of Tetany may occasionally occur in an advanced case

SKIN The patient may have a dusky or muddy complexion Patchy pigmentation may appear over the malar regions forehead and buttocks There may be follicular hyperkeratosis The nails tend to be brittle and ridged Clubbing of fingers may be present

HÆMOPOIETIC SYSTEM Anæmia is not apparent until the disease has progressed for several months In early phases anæmia is slight and the red cells are normal or slightly smaller than normal with or without evidence of hypochromia In a full blown form there is frank macrocytosis though colour index is not always increased due to associated iron deficiency Red cells may show marked variation in shape and size with the appearance of a few polychromic stippled and nucleated red cells In untreated cases the reticulocyte count is within normal limits varying from 0 4 to 2 per cent Occasionally blood smear may show megaloblasts and/or macropolycytes The white cells are reduced in number with evidence of neutropenia and relative lymphocytosis Platelets may be decreased to a variable extent Hypoprothrombinæmia may result from impaired absorption of vitamin K.

Other characteristics are low bloodpressure fast pulse and reduced

basal metabolic rate In advanced cases wasting of muscles is extreme and there is no subcutaneous fat Purpuric spots may appear and signs of protein deficiency *viz* œdema of legs or dehydration resulting from water and salt deficiency may supervene in the later stage

LABORATORY DATA

Blood Picture The blood picture in a well developed case may be as follows Hæmoglobin—6 g per cent R B C—1 500 000/c mm Reticulocytes—0 4 per cent P C V—19 per cent M C V—125 c micron M C H—44γγ M C H C—32 per cent M D—8 5 micron Price Jones curve shows a peak shifted to the right and a spreading of the base Total W B C—3 400/c mm Neutrophil 40 per cent lymphocyte 56 per cent monocyte 3 per cent eosinophil 1 per cent Platelets—110 000/c mm

Bone marrow In the anæmic cases the marrow is cellular and megaloblastic In the granular series giant metamyelocytes and macropolycytes are seen Megakaryocytes are reduced and show diminished activity

Blood Biochemistry Serum vitamin B_{12} level may be lower than 100 micromicrogram per ml (normal values 100 to 600) and serum iron reduced (normal values 60—140 microgram per 100 ml) In a well developed case there are evidences of impaired absorption of all the three important hæmopoietic substances *viz* folic acid vitamin B_{12} and iron

Hypoproteinæmia with hypoalbuminæmia is a common feature in an advanced case The serum lipids are diminished and may remain so even after clinical control suggesting thereby that the malabsorption is probably not the sole responsible factor this may imply other as yet undermined metabolic defects involved in lipid synthesis The fasting blood sugar may be low and the post absorptive curve after glucose is flat The serum cholesterol calcium potassium and phosphorus may also be low indicating malabsorption of minerals and fat soluble vitamin D Vitamin A and carotene levels in serum tend to be reduced

Gastric Analysis The acid curve is variable There may be achlorhydria with or without response to histamin With improvement of blood picture acid secretion returns in achlorhydric cases

Radiological Findings Barium meal shows alteration in the outline of mucosal folds of the small intestine The normal feathery pattern is lost and instead there is abnormal segmentation associated

with diminished motility or there may be coarse granular appearance with areas of flocculation dispersed irregularly due to excessive mucus secretion The lumen of the small intestine is commonly dilated depending on the severity of the disease If the condition is severe the obliteration of the valvulæ conniventes may make the bowel look like a tube into which wax has been poured and allowed to harden (*Moulage sign*) There may be evidence of intestinal hurry During remission the pattern tends to return to normal

ABSORPTION TESTS

Faulty intestinal absorption may be demonstrated by combinations of absorptive tests

(*a*) *Glucose Tolerance* The glucose curve after the ingestion of 50 g of glucose is often a flat type due to impaired absorption whereas after intravenous injection of 50 g glucose it shows a sharper rise and less rapid fall than normal due to decreased glucose tolerance consequent on carbohydrate deprivation Variations in gastric emptying time glucose utilisation and the possible occurrence of flat curves in normal subjects render the oral test of doubtful value in diagnosis of sprue

(*b*) *Vitamin A Absorption* Following the ingestion of 300 000 international units of vitamin A in the form of fish liver oil concentrate the serum value is less than 85/g at 5 hours whereas the normal values are higher

(*c*) *Radio active Vitamin B_1 Absorption* This study reveals impaired absorption of vitamin B_1 unaffected by gastric intrinsic factor or antibiotic thus differentiating the condition from pernicious anæmia and intestinal stasis syndrome

(*d*) *Xylose Excretion* The urinary excretion of D Xylose a pentose sugar which is not metabolised in the body has been used as a test of sugar absorption The mean urinary excretion of D xylose in 5 hours after an oral dose of 25 g in sprue is usually less than 4 g the normal being over 5 g

(*e*) *Sucrose Absorption* Patients with sprue excrete significantly greater quantities of intact sucrose in urine after an oral dose of 25 g sucrose than do normal subjects The urine of a normal person becomes free from sucrose after a 10 hour fast but sprue patients may exhibit sucrosuria throughout a 24 hours fast Diminished hydrolysis of sucrose and increased intestinal permeability are possible explanations

(*f*) *Fæcal Determination* (See page 440) This is done after putting the patient on a known amount of fat (100 g) daily for 3 days Fat balance test may also be done

(*g*) *Nicotinic Acid Test* Normal hot sensation after 150 mg of nicotinic acid by mouth is not experienced by a sprue patient

DIAGNOSIS

A typical case with glossitis anæmia and steatorrhœa is easily diagnosed However milder cases without obvious steatorrhœa and anæmia are apt to be missed For detection of tropical sprue the following points need consideration

CLINICAL DATA (1) Middle aged person with long history of yearly morning afebrile diarrhœa (2) Pale bulky and frothy stool (3) Glossitis or soreness of the mouth (4) Progressive loss of weight with anæmia (5) Doughy distended abdomen out of proportion to the tympany

It should be remembered that relative prominence of certain features varies from case to case For example the signs of sprue may involve almost exclusively the tongue or bowel (*Incomplete sprue*)

LABORATORY DATA (1) Hæmatological examination shows in a severe case macrocytic anæmia with megaloblastic arrest of bone marrow (2) Stool analysis reveals increased total fat with high fraction of fatty acid (3) Blood biochemistry—(*a*) low fasting blood sugar (*b*) hypocalcæmia (*c*) hypocholesterolæmia (*d*) low plasma protein with hypo albuminæmia (4) Fractional test meal shows presence of hydrochloric acid or achlorhydria with response to histamin (5) Absorption studies—(*a*) flat sugar curve on oral glucose tolerance test (*b*) impaired absorption of vitamin B_{12} uninfluenced by intrinsic factor or antibiotic (*c*) impaired absorption of vitamin A (*d*) diminished xylose excretion (*e*) increased urinary excretion of sucrose after oral administration (*f*) nicotinic acid test—no reaction

RADIOLOGICAL DATA Evidence of functional deficiency states of *the intestine after opaque meal*

DIFFERENTIAL DIAGNOSIS

Sprue presents features of malabsorption in general Hence the differential diagnosis is made on the following lines

Firstly malabsorption syndrome must be distinguished from other disorders which may give rise to similar manifestations *viz* anæmia and diarrhœa

Secondly having established the diagnosis of malabsorption yndrome an attempt should then be made to determine whether it is primary or secondary

Lastly if it is primary the tropical and non tropical varieties and cœliac disease hould be differentiated

A DISORDERS SIMULATING SPRUE Non steatorrhœal diseases which may closely re emble sprue clinically

Pernicious Anæmia (rare in the tropics) (1) There is no steatorrhœa (2) Features of sub acute combined degeneration may be present (3) Irreversible histamin fast achlorhydria (4) Normal glucose absorption curve (5) Deficient ab orption of radio active vitamin B_1 which is corrected by simultaneous administration of intrinsic factor

Nutritional Macrocytic Anæmia (1) Clinical history suggesting dietary inadequacy and absence of steatorrhœa (2) Radio active vitamin B_{12} absorption is normal

Carcinoma of the Stomach (1) Occurs in elderly individual (2) Rapidly progressing cachexia and anæmia (3) A mass may be palpable (4) Roentgenological evidence of filling defect in the stomach (5) Malignant cells in the gastric contents

Pellagra (1) Absence of steatorrhœa (2) Presence of symmetrical dermatitis (3) Psychic disturbances

Giardiasis (1) Stools in some cases are pale showing *Giardia intestinalis* (2) Response to specific treatment

B SECONDARY MALABSORPTION SYNDROME The secondary malabsorption syndrome may be pancreatogenous hepatogenous or enterogenous

Pancreatic Steatorrhœa (1) Neutral or unsplit fat is mostly present in stools (2) Episodes of pain (3) Pancreatic calcification or diabetes (4) Excessive loss of nitrogen in stool

Hepatogenous Steatorrhœa (1) Features of obstructive jaundice *viz* acholic stool pruritus bradycardia excessive conjugated bilirubin in serum with presence of bile in urine and no urobilinogen (2) History of colicky pain with intermittent jaundice (suggestive of gallstone) (3) Progressively increasing jaundice with a palpable gall bladder (in an elderly person indicates carcinoma of the head of the pancrea)

Enterogenous Steatorrhœa May be due to a number of condition

such as tuberculous enteritis regional ileitis Whipple s disease lymphomatous disorders scleroderma and anastomotic syndromes However full clinical history physical and x ray findings are helpful in detecting them Whipple s disease cannot be diagnosed definitely without a histological study of the small intestine and mesenteric lymphglands A suspicion may however be made when sprue syndrome occurs with history of abdominal pain fever discolouration of skin and swelling of joints

C PRIMARY MALABSORPTION SYNDROME In both tropical and non tropical sprue but not in cœliac disease a sore mouth and macrocytic anæmia are commonly encountered Idiopathic steatorrhoea (in adults) and cœliac disease (in children) occur specially in the *temperate regions* Tropical sprue responds well to the *treatment with* folic acid but the other two do not Children with cœliac disease have hypochromic anæmia and do well if wheat flour is excluded from the diet while in tropical sprue there is no intolerance to wheat and rye glutens

PROGNOSIS

Tropical sprue is no longer a dreaded disease The prognosis is good provided adequate treatment and appropriate diet are given early Remissions are maintained with proper care Severe cases of long duration may require treatment for an indefinite period Relapses may occur Cachexia infection hæmorrhage and potassium deficiency are unfavourable features The character of stools dyspeptic symptoms and blood condition provides satisfactory guides to therapy Much depends on the co-operation of the patient and the facilities for treatment

SPECIFIC TREATMENT

ANTI ANÆMIC DRUGS Folic acid vitamin B_{12} and liver extract have been specific therapeutic agents in tropical sprue

Folic acid is the drug of choice It is given orally It is also available in 15 mg ampoules for parenteral administration

Dosage 5 to 10 mg thrice daily for a month followed by a maintenance dose of 5 10 mg daily until the clinical and hæmatological recovery Even cases without anæmia respond to folic acid The stools become normal the patient s appetite increases and he gains in weight Recurrences are treated in the same way

Vitamin B_1 is used as an alternative in a daily dose of 15 50 micro grams intramuscularly for 2 weeks and then every other day for 2 weeks

Thereafter it may be given fortnightly There is no adequate information to determine if parenteral administration of vitamin B_{12} has any advantage over the accepted preference for folic acid However persistent low serum levels of vitamin B_{12} during folic acid therapy calls for its administration In fact combination therapy of folic acid and vitamin B_{12} has been advocated by some

Concentrated liver extract has also been used intramuscularly Crude preparations containing different members of vitamin B complex in addition to the full quota of hæmopoietic principle are definitely better than refined ones A potent preparation in a dose of 4 c cm daily for 6 days followed by 4 c cm on alternate days for one month should be given in an average case for the desired clinical and hæmatological improvement

GENERAL MANAGEMENT

Physical and mental rest are helpful in establishing early remissions Emphasis should be put on treating the patient as a whole rather than on a single therapeutic measure In severe cases the patients should remain in bed If dehydrated and unable to take enough fluid saline and glucose should be given intravenously Those complicated with severe anæmia and hypoproteinæmia will need blood transfusions Associated infection and conditions should be sought for and treated with appropriate antibiotics

DIET The diet should be high in good proteins low in fats and carbohydrate roughly in proportion of 1 0 3 1 3 instead of normal 1 1 5 ratio Many of the strict special diets used in the past are no longer deemed necessary in an average case if specific therapy is given The source of protein should be lean meat or fish while skimmed milk or butter milk small quantities at a time may be suitably arranged according to the individual patient his tolerance and response as judged by appearance of the stool and abdominal symptoms The diet should be bland non irritating with low residue If the patient cannot take or tolerate enough food he is given a diet which at the beginning is basically skimmed milk to which other articles are added in stages to make up ultimately a good mixed diet the total calories beginning with about 1000 and worked up to about 3000 per day according to the progress of the case Such vegetables as green papaya or plantain are preferable to coarse articles Butter cream fried articles and excess of starch are avoided If constipated *Bael* and *Isaphghula* are helpful Brisk purgatives are better avoided

SYMPTOMATIC TREATMENT

Persistent diarrhœa and abdominal symptoms may benefit from sulphaguanidine or antibiotic therapy Bismuth and koalin may also be given

Iron salts (ferrous sulphate gr 6 t d s) are given by mouth if there is evidence of deficiency

Dilute hydrochloric acid ½ to 1 dr in sufficient water is sipped with or after the principal meals if the gastric acid is low or absent

Sodium and potassium salts as well as vitamin B complex and vitamins A & D may be required to correct asthenia and meet the deficiencies

For glossitis and stomatitis weak Condy s gargle and boroglycerin or mercurochrome paint are given along with administration of nicotinamide (200 mg) and riboflavin (10 mg) daily

Tetany needs treatment with calcium injections and concentrated vitamin D

For flatulence charcoal or carminatives are indicated along with restriction of sugar

Adrenal steroids may have a place in selected stubborn cases but are not ordinarily used

Complications are treated appropriately e.g. sulphonamide or streptomycin for *Esch coli* infection of the urinary tract vitamin K for petechial hæmorrhages etc

CONVALESCENCE

It should be slow Well balanced diet adequate in protein and vitamin should be continued for an indefinite period Alcohol rich spiced and sugary food are avoided Change of climate is often advantageous but not essential

PREVENTIVE MEASURES

As the cause of prue is not quite clear there is no satisfactory method of prevention Well balanced diet with inclusion of animal protein may have a prophylactic value Any bowel infection should be immediately attended to Excess of fat is avoided At the earliest sign of relapse or recurrence folic acid therapy should be resumed together with dietetic control

R N CHAUDHURI

APPENDIX

DIAGNOSIS OF FEVERS IN THE TROPICS

Of all the diseases that baffle the clinical acumen and experience of even the best of physicians in the tropics fevers form the most important group For a proper diagnosis as to the nature of a febrile disease it is essential that a *careful history taking* and a *thorough examination* should always be made Here we would deal with the main points necessary for an accurate diagnosis

History of the Present Illness

FEVER *Mode of Onset* Sudden or gradual

Sudden onset

- Malaria
- Blackwater fever
- Influenza
- Pneumonia
- Cerebrospinal meningitis
- Acute bacillary dysentery
- *Esch coli* infection of the urinary tract
- Smallpox
- Measles
- Dengue
- Septicæmia
- Filarial lymphangitis
- Acute tonsillitis
- Acute otitis media
- Mastoiditis
- Rheumatic fever
- Acute bacterial endocarditis
- Heat hyperpyrexia
- Plague
- Rat-bite fever
- Relapsing fevers
- Typhus fevers
- Leprotic fever
- Serum reaction
- Suppurative pylephlebitis

Gradual onset

- Typhoid and paratyphoid fevers
- Kala azar
- Bronchopneumonia
- *Esch coli* infection
- Diphtheria
- Pleural effusion
- Tuberculosis
- Amœbic hepatitis and liver abscess
- Infectious hepatitis
- Chickenpox
- Tuberculous meningitis
- Acute miliary tuberculosis
- Subacute bacterial endocarditis
- Epidemic dropsy
- Bronchiectasis
- Typhus fevers
- Acute cholecystitis
- Acute leukæmias (early stage)
- Focal infections
- Malignant disease

Nature Remittent or intermittent

Remittent	*Intermittent*
Typhoid and paratyphoid fevers	Malaria
Malignant tertian malaria	Kala azar
Kala azar	Blackwater fever
Influenza	Filariasis
Pneumonia	*Esch coli* infection of the urinary tract
Bronchopneumonia	Epidemic dropsy
Dengue	Pulmonary tuberculosis
Diphtheria	Localised pyogenic infections
Meningitis	Visceral syphilis
Septicæmias	Subacute bacterial endocarditis
Acute bacillary dysentery	Septicæmias
Pleural effusion	
Pulmonary tuberculosis	
Acute miliary tuberculosis	
Liver abscess	
Bacterial endocarditis	
Rheumatic fever	
Epidemic dropsy	
Ascariasis	
Encephalitis	
Relapsing fevers	
Typhus fevers	
Plague	
Undulant fever (Malta fever)	

Duration Any febrile disease in the tropics that is continued for more than seven days should be suspected to be typhoid or paratyphoid fever Other causes of prolonged fever are malaria kala azar unresolved pneumonia bronchopneumonia *Esch coli* infection of the urinary tract hepatic abscess or other localised suppurative processes pleural effusion pulmonary tuberculosis glandular tuberculosis tuberculous meningitis tuberculous peritonitis subacute bacterial endocarditis malignant tumours hyperthyroidism visceral syphilis and nervous pyrexia.

Height of Temperature The occurrence of *high temperature in the beginning of the illness* is a characteristic of all fevers with sudden onset *Hyperpyrexia* may develop in the following

Malaria (benign tertian)	Pontine hæmorrhage
Pneumonia	Heat hyperpyrexia

Cerebrospinal fever	Rheumatic fever (very rarely)
Septicæmia	Tetanus (rarely)

Periodicity Periods of pyrexia alternating with apyrexial intervals are met with in

- Malaria (benign tertian and quartan)
- Kala azar
- Relapses of typhoid and paratyphoid fevers
- Pulmonary tuberculosis
- Relapsing fevers
- Subacute bacterial endocarditis
- Rat bite fever
- Hodgkin s disease with the Pel Ebstein syndrome
- Chronic myeloid leukæmia
- Undulant fever

Double Rise A temperature chart showing double rise in twenty four hours is suggestive in order of frequency of the following

Kala azar	Pulmonary tuberculosis
Malaria	Acute and subacute bacterial endocarditis
Liver abscess	
Typhoid fever	*Esch coli* infection of the urinary tract

CHILLS OR RIGORS Chills or rigors are associated with the sudden rise of temperature in any febrile disease Chills may occur at the very beginning of the rise or may be of recurrent nature

At the beginning	*Recurrent*
Malaria (benign tertian)	Malaria (benign tertian)
Pneumonia	Filarial fever
Influenza	*Esch coli* infection of the urinary tract
Smallpox	
Cerebrospinal meningitis	Influenza
Septicæmia	Septicæmia
Pyelonephritis	Acute bacterial endocarditis
Filariasis	Localised pyogenic infection such as empyema cholangitis perinephric abscess hepatic abscess appendicular abscess subphrenic abscess pelvic abscess antral suppuration suppurative mastoiditis and osteomyelitis
Rat bite fever	
Bacterial endocarditis	
Plague	
Typhus fevers	
Undulant fever	
Suppurative pylephlebitis	

SWEATING Presence of marked sweating during the remission or intermission of the temperature is characteristic of the following

Pulmonary tuberculosis	Bacterial endocarditis
Malaria	Paratyphoid fever (not uncommonly)
Influenza	Typhoid fever (occasionally)
Rheumatic fever	Tetanus
Cerebrospinal meningitis	Relapsing fevers
Pyelonephritis	Undulant fever
Localised suppurative processes	Septicæmia

It should be remembered that *sweating* often occurs in any febrile disease treated with *quinine salicylate other antipyretics* or *sulpha drugs*

VOMITING Repeated vomiting with the onset of fever in the adults occur in the following

Malaria	Plague
Blackwater fever	Relapsing fevers
Cerebrospinal meningitis	Acute appendicitis
Influenza	Acute pyelonephritis
Smallpox	Acute pancreatitis

GENERALISED PAINS IN THE BODY They are found in the following

Influenza	Poliomyelitis
Dengue	*Encephalitis*
Malaria	Weil s disease
Smallpox	Rat bite fever
Cerebrospinal meningitis	Relapsing fevers
Septicæmia	Plague
	Trichinosis

MENTAL STATE *Coma* sets in rapidly in the following diseases

Cerebral malaria	Septicæmia
Cerebrospinal meningitis	Plague
	Heat hyperpyrexia

Cerebral hæmorrhage—in this case the unconsciousness precedes the rise of temperature

Early delirium is associated with the following

Cerebral malaria	Septicæmia
Cerebrospinal *meningitis*	*Dengue*

Pneumonia (especially in alcoholics)
Severe cases of acute bacillary dysentery
Smallpox
Heat hyperpyrexia
Plague
Rat bite fever
Typhus fevers

CONVULSIONS The occurrence of *convulsions at the onset* is suggestive of the following diseases

Cerebral malaria
Cerebrospinal meningitis
Apical pneumonia
Cerebral thrombosis
Poliomyelitis
Heat hyperpyrexia
Tetanus

It should be emphasized in this connection that convulsions in children frequently occur due to a reflex irritation from any source and hence are not of the same significance as in adults

HEADACHE Severe headache in the early stages is associated with the following

Malaria
Cerebrospinal meningitis
Typhoid fever The headache of typhoid fever disappears after the first week
Smallpox
Dengue
Weil s disease
Encephalitis
Plague
Influenza

SORE THROAT It is complained of in the following

Acute tonsillitis
Diphtheria
Rheumatic fever
Influenza
Secondary syphilis
Acute leukemias
Agranulocytosis
Scarlet fever (rare)

HEMORRHAGES The occurrence of hemorrhages into the skin and from the mucous membranes in the invasive stage of fever is a grave sign which may occur in the following

Hemorrhagic smallpox
Cerebrospinal meningitis
Hemorrhagic measles
Malignant diphtheria
Septicemias
Plague
Typhus fever
Rat bite fever
Weil s disease

The onset of influenza typhoid fever kala azar and dengue may be heralded by an *epistaxis* Typhoid fever in children is sometimes

ushered in by *hæmaturia* *Hæmaturia* is not uncommon in *Esch coli* infections of the urinary tract

HÆMOGLOBINURIA The passage of dark port wine coloured urine with the onset of fever is diagnostic of blackwater fever Paroxysmal hæmoglobinuria may be due to syphilitic infection

DIARRHŒA The occurrence of diarrhœa in the early stages of fever suggests the following

Acute bacillary dysentery	Measles
Malignant malaria	Heat hyperpyrexia
Apical pneumonia	Bacterial food poisoning
Paratyphoid fever	Epidemic dropsy
Influenza	

FREQUENCY OF MICTURITION It suggests the following febrile conditions

Cystitis	Retrocæcal appendicitis
Pyelonephritis	Heat hyperpyrexia (prodromal stage)
Tuberculosis of the kidney	

History of Past Illnesses

The occurrence of the following illnesses in the past should be definitely enquired into

Dysentery	Filariasis
Malaria	Syphilis
Blackwater fever	Pleural effusion
Kala azar	Rheumatic fever
Typhoid fever	Tonsillitis
Paratyphoid fever	Carbuncles and boil
Smallpox	Hæmoptysis
Measles	Recurrent attacks of influenza

It is worth noting that second attacks of smallpox chickenpox and measles are very rare A history of recurrent attacks of influenza should make one suspect of pulmonary tuberculosis

Family History

It is of importance to know whether any member of the family had suffered or has been suffering from any one of the following

Pulmonary tuberculosis	Typhoid fever
Malaria	Measles

Kala azar	Smallpox
Blackwater fever	Chickenpox
Filariasis	Epidemic dropsy

Personal History

ENVIRONMENT An enquiry should be made regarding residence in the tropics or in endemic areas of malaria filariasis plague or typhus fevers Information should be sought as to the occurrence of an epidemic in the locality The possibility of certain epidemic diseases in a particular area should be kept in mind

OCCUPATION Occupations entailing prolonged work in a hot and humid environment are likely to produce heat hyperpyrexia Grooms and farmers are liable to develop actinomycosis Sewer workers fish cleaners sugar cane workers and durwans living in the basement of old houses are liable to Weil s disease

HABITS Addiction to excess of alcohol tobacco and other intoxicants should be interrogated

General Examination

Apart from decubitus nutrition build muscular development and facies the following points should be noted

TOXÆMIA Little or no toxæmia in presence of moderately high fever points to

Esch coli infection of the urinary tract	Localised suppurative processes
Acute kala azar	Leukæmias
Glandular tuberculosis	Hodgkin s disease

EMACIATION Early rapid emaciation occurs in the following febrile diseases

Acute bronchopneumonic or miliary tuberculosis	Malignant disease
Cerebro spinal meningitis	Graves s disease

HERPES LABIALIS The appearance of herpes labialis with the onset of fever is indicative of the following

Common cold	Cerebro spinal fever
Malaria	Weil s disease
Pneumonia	Paratyphoid fever

ushered in by *hæmaturia* *Hæmaturia* is not uncommon in *Esch coli* infections of the urinary tract

HÆMOGLOBINURIA The passage of dark port wine coloured urine with the onset of fever is diagnostic of blackwater fever Paroxysmal hæmoglobinuria may be due to syphilitic infection

DIARRHŒA The occurrence of diarrhœa in the early stages of fever suggests the following

Acute bacillary dysentery	Measles
Malignant malaria	Heat hyperpyrexia
Apical pneumonia	Bacterial food poisoning
Paratyphoid fever	Epidemic dropsy
Influenza	

FREQUENCY OF MICTURITION It suggests the following febrile conditions

Cystitis	Retrocæcal appendicitis
Pyelonephritis	Heat hyperpyrexia (prodromal stage)
Tuberculosis of the kidney	

History of Past Illnesses

The occurrence of the following illnesses in the past should be definitely enquired into

Dysentery	Filariasis
Malaria	Syphilis
Blackwater fever	Pleural effusion
Kala azar	Rheumatic fever
Typhoid fever	Tonsillitis
Paratyphoid fever	Carbuncles and boils
Smallpox	Hæmoptysis
Measles	Recurrent attacks of influenza

It is worth noting that second attacks of smallpox chickenpox and measles are very rare A history of recurrent attacks of influenza should make one suspect of pulmonary tuberculosis

Family History

It is of importance to know whether any member of the family had suffered or has been suffering from any one of the following

Pulmonary tuberculosis	Typhoid fever
Malaria	Measles

Generalised	*Localised*
Typhus fevers	Rat bite fever
Syphilitic lymphadenitis	Lymphogranuloma inguinale
	Gonococcal infection

CLUBBING OF FINGERS This condition is met with in the following febrile diseases

Bronchiectasis	Chronic empyema
Pulmonary tuberculosis (fibroid type)	Liver abscess
Lung abscess	Subacute bacterial endocarditis

ŒDEMA One should look for œdema of the legs and feet and also for cutaneous erythema to make a diagnosis of the following

Filarial elephantiasis	Epidemic dropsy

CUTANEOUS NODULES They are present in leprosy dermal leishmanoid epidemic dropsy rheumatic fever rheumatoid arthritis and cysticercosis

ACUTE ARTHRITIS The early occurrence of arthritis is suggestive of the following febrile diseases

Rheumatic fever	Acute bacterial endocarditis
Rheumatoid arthritis	Cerebro spinal meningitis
Gonococcal infection	Acute gout
Septicæmia	Acute leukæmias
	Undulant fever

RASHES The occurrence of rashes their nature time and order of appearance and their evolution will clarify the diagnosis in most cases of fever (*See* Table on page 463)

PULSE The pulserate should be taken in every case of fever and it should be correlated with the oral temperature For each degree of rise of oral temperature the pulserate in the adults increases by 8 10 beats With a temperature of 100°F the pulse rate is expected to be above 96

Relative bradycardia is a valuable sign and is seen in the early stage of the following febrile diseases

Typhoid fever	Malaria occasionally
Paratyphoid fever	Apical pneumonia occasionally
Uncomplicated influenza	Weil disease
Dengue	Typhus fever

OCULO-NASOPHARYNGEAL CATARRH The signs of catarrh of the upper respiratory tract are present in

Influenza	Common cold
Measles	Cerebrospinal meningitis
Whooping cough	

PALLOR AND ANÆMIA Rapid onset of pallor and anæmia in course of a febrile illness occurs in the following diseases

Blackwater fever	Kala azar
Malaria (malignant tertian)	Liver abscess
Septicæmia (streptococcal)	Hodgkin s disease
Acute leukæmias	Acute bacterial endocarditis

JAUNDICE The early occurrence of even a slight jaundice is very helpful in the diagnosis of the following conditions

Infectious hepatitis	Influenza
Malignant malaria	Relapsing fevers
Blackwater fever	Weil s disease
Septicæmia	Yellow fever
Pneumonia occasionally	Paratyphoid fever occasionally
	Liver abscess rarely

CYANOSIS It is due to the presence of excess of reduced hæmoglobin in blood (5 g or over per 100 c cm of blood) It may be present in the following febrile diseases

Pneumonia	Spontaneous pneumothorax
Bronchopneumonia	Acute spasmodic bronchitis
Malignant influenza	Cardiac failure of epidemic dropsy
Pleural effusion	
Pulmonary infarction	Acute miliary tuberculosis

GLANDULAR ENLARGEMENT Enlargement of the lymphnodes associated with a febrile illness is found in the following

Generalised	*Localised*
Tuberculous lymphadenitis	Filarial infection
Lymphatic leukæmia	Syphilitic infection
Septicæmia	Pyogenic infection
Hodgkin s disease (Pel Ebstein syndrome)	Soft chancre
	Glandular fever
Glandular fever	Plague (bubonic)
Rat bite fever	Leprosy
Undulant fever	Tick borne typhus

Moderate enlargement indicates

- Chronic malaria
- Kala azar
- Splenic anæmia
- Tropical splenomegaly
- Hodgkin s disease
- Portal cirrhosis (hepatic)
- Lymphatic leukæmia
- Syphilis
- Amyloid disease
- Infarction
- Hydatid cyst

Marked enlargement indicates

- Tropical splenomegaly
- Chronic malaria (quartan and benign tertian)
- Splenic anæmia
- Chronic kala azar
- Myeloid leukæmia

Liver In presence of an *enlarged liver* the following febrile diseases may be kept in mind

- Chronic kala azar
- Malignant tertian malaria
- Paratyphoid fever
- Acute hepatitis
- Liver abscess
- Infectious hepatitis
- Weil s disease
- Infantile biliary cirrhosis
- Syphilis
- Malignant disease
- Hepatic cirrhosis
- Hodgkin s disease
- Leukæmia
- Suppurative hydatid cyst
- Amyloid disease

Tender and enlarged liver It is found in the following febrile conditions

- Amœbic hepatitis
- Hepatic abscess
- Infectious hepatitis
- Malignant tertian malaria
- Blackwater fever
- Typhoid and paratyphoid fevers
- Acute or subacute hepatic necrosis
- Cholangitis
- Acute lymphatic leukæmia
- Weil s disease
- Yellow fever

Ascites The causes of ascites in association with fever are

- Tuberculous peritonitis
- Hepatic cirrhosis
- Hepatic abscess
- Acute diffuse nephritis
- Tropical splenomegaly
- Splenic anæmia
- Peritoneal carcinomatosis
- Carcinoma of the liver

EXAMINATION OF CERTAIN SPECIAL SITES In fevers of obscure origin particular care should be taken to examine the mouth for the Koplik s spots of measles the teeth for apical dental abscess throat

Cerebro spinal meningitis
Cerebral abscess
Undulant fever
Mumps

A disproportionately rapid pulse rate usually occurs in the early stage of the following fevers

Pulmonary tuberculosis
Malaria
Blackwater fever
Pneumonia
Rheumatic fever
Acute bacillary dysentery
Plague
Typhus fevers

RESPIRATION The normal rate of respiration in adults is 18 20 per minute The pulse respiration ratio is 4 1 The presence of dyspnœa with rapid respiration indicates the following

Pneumonia and broncho pneumonia
Pleural effusion
Laryngeal diphtheria
Spontaneous pneumothorax
Acute miliary tuberculosis
Pulmonary infarction
Epidemic dropsy with cardiac failure
Acute anterior poliomyelitis
Acute ascending paralysis (Landry s type)
Heat hyperpyrexia
Pneumonic plague

Systemic Examinations

A routine examination of the various systems such as the respiratory circulatory and the nervous will reveal the *localising signs* which will be of great value in the diagnosis of fevers *e g* pneumonia pleural effusion pulmonary tuberculosis bacterial endocarditis rheumatic carditis meningitis Here we shall deal with febrile conditions which do not present any definite localising signs In all such cases alimentary system should be examined first

ABDOMINAL EXAMINATION The abdomen should be especially examined for enlargement of the spleen liver and gall bladder tenderness over the same organs the appendix colon and kidneys presence of thickened colon omentum and abnormal masses such as enlarged mesenteric or iliac lymphnodes and cystic tumours of the kidneys ovaries and the retroperitoneal tissues A careful search should be made for evidences of free fluid in the peritoneal cavity (*ascites*)

Spleen Early and slight enlargement usually indicates the following

Typhoid and paratyphoid fevers
Malignant tertian malaria
Blackwater fever
Acute kala azar
Septicæmias
Acute bacterial endocarditis
Relapsing fevers

In every case of fever in the tropics stained bloodsmear by the thick and thin film methods should be repeatedly and carefully examined for malaria parasites It is worth remembering that the absence of malaria parasites from the blood film on a single examination does in no way exclude the diagnosis of malaria

Special Investigations

In obscure cases of pyrexia the following special investigations are essential

EXAMINATION OF THE CEREBROSPINAL FLUID It is essential in cases of fever associated with early onset of delirium coma and signs of meningeal irritation

BLOOD EXAMINATION The blood may have to be especially examined for

Leishman Donovan bodies	*P pestis*
Microfilariæ	*Spirillum minus*
Trypanosomes	

BLOOD-CULTURE This is done for the detection of the causative organisms

SERUM AGGLUTINATION TESTS These are done for the diagnosis of typhoid or paratyphoid fever typhus fevers undulant fever glandular fever (for the presence of heterophil antibodies) and Weil s disease

EXAMINATION OF THE MATERIAL FROM STERNAL PUNCTURE It is done for L D bodies malaria parasites leukæmias

EXAMINATION OF THE MATERIAL FROM GLAND PUNCTURE This is done for diagnosis of bubonic plague filariasis syphilis and trypanosomiasis

BIOPSY OF GLANDS This investigation is especially helpful in the diagnosis of Hodgkin s disease tuberculous lymphadenitis lymphatic leukæmia and lymphosarcoma

RADIOLOGICAL EXAMINATION OF THE CHEST For the diagnosis of the early phases of pulmonary tuberculosis lung abscess interlobar empyema bronchial obstruction by a foreign body and hepatic abscess radiological examination of the chest is done

RADIOGRAPHS OF THE TEETH AND NASAL SINUSES A small apical abscess of the teeth may cause low intermittent fever So radiographs of the teeth and nasal sinuses are necessary

for tonsillitis and faucial diphtheria the mastoid region for evidence *of acute mastoiditis the ears for acute otitis media* the nasal sinuses for evidence of suppuration the spine for tuberculous disease the axillæ for abscess and lymphadenitis the renal areas for pyelonephritis and perinephric abscess the spermatic cord and epididymis for acute funiculitis the ischiorectal fossæ for deep seated abscesses the rectum for proctitis perirectal and prostatic abscesses and the metaphysis of long bones for osteomyelitis A vaginal examination in the females is necessary to exclude inflammatory diseases of the uterus the fallopian tubes and the ovaries

Laboratory Investigation

In the diagnosis of fevers without any localising signs various laboratory aids such as blood examination hæmoculture serum agglutination tests macroscopic microscopic and cultural examination of urine stools and sputum are often very helpful

Blood Examination An examination of the blood for a total and a differential count of the white blood cells is a simple and yet a very valuable test

The presence of a definite *leucopenia* (a white cell count below 5 000 per c mm) is strongly suggestive of the following febrile conditions

- Typhoid fever
- Paratyphoid fever
- Kala azar
- Chronic malaria
- Influenza
- Dengue
- Sandfly fever
- Acute miliary tuberculosis
- Measles

A definite *leucocytosis* (white cell count over 10 000 per c mm) is met with in

- Pneumonias
- Cerebrospinal meningitis
- Acute bacillary dysentery
- Localised suppurative processes
- *Septicæmias*
- Diphtheria
- Rheumatic fever
- Amœbic hepatitis and liver abscess
- Pyelonephritis
- Leukæmias
- Hodgkin s disease
- Glandular fever
- Plague
- Typhus fevers
- Weil s disease
- Relapsing fevers
- Acute bacterial endocarditis
- Acute appendicitis
- Acute cholecystitis
- Smallpox

TABLE SHOWING THE CHARACTERISTICS OF RASHES IN FEBRILE DISEASES

Disease	*Day of appearance*	*Order of appearance*	*Character*	*Evolution*
Cerebrospinal meningitis	1st to 2nd day	Trunk neck and limbs	Petechial purpuric or roseolar	
Chickenpox	1st day	First on trunk and scalp Scanty on face and distal part of limbs	Vesicular	Rapid evolution into pustule within 48 hours
Dengue	4th to 5th day	First on the wrist then on the trunk thighs and legs	Measly	Disappears by scaly desquamation in 2 3 week
Measles	4th day	First on the forehead along the hairy margin the face trunk and limb	Maculo papular	Macules coalesce and form crescentic erythematous patches Disappear by fine desquamation in course of 2 3 days
Rat bite fever	6 weeks after the bite	Face trunk and limbs	Erythematous papular or urticarial	Disappear slowly
Secondary syphilis	6-8 weeks after the primary sore	Trunk and flexor aspects of arms Face usually escape	Macule coppery papules rarely pustule often polymorphic	
Serum reaction	8 12 day after injection of serum	May appear first about the site of injection and then spread over the whole body	Mainly erythematous or urticarial	The rash often disappears in a few hour
Smallpox	3rd to 4th day	First on the forehead wrist and hands	Macular papular and then vesicular	Maculo papular—3rd to 4th day Vesicles—5th to 6th day Pustules—9th day Crusts—10th to 12th day
Typhoid fever	6th to 10th day	*First over the abdomen* and chest and then over the limb	*Roseolar*	Disappear on pressure The rash appear in successive crops each lasting for 2 4 days
Typhus fevers	4th day	First in the axillae and over wrists then over abdomen chest and the limb	Patchy erythematous patches	Pink papules petechial on the 8th day

WASSERMANN REACTION The test should be carried out as a routine in all cases of prolonged pyrexias of unknown origin Kahn test is also useful for this purpose

GUINEAPIG INOCULATION TESTS They are helpful in the diagnosis of spirochætal fevers

EXPLORATORY PLEURAL PUNCTURE It is necessary for the definite diagnosis as to the nature of a pleural effusion

THERAPEUTIC TESTS Response to treatment by certain specific remedies may help in the diagnosis of certain fevers *e g* malaria by its response to quinine or other special drugs amœbic hepatitis by rapid improvement under emetine injections rheumatic infection by prompt response to salicylates rat bite fever responding to injections of novarsenobillon and masked hyperthyroidism to oral administration of Lugol s iodine solution or thiouracil derivatives

(ii) *Non specific* Acute infective diarrhœa of infants and children chronic ulcerative colitis

(b) *Protozoal*—Ciliate flagellate amœbic malarial leishmanial

(c) *Helminthic*—Hookworm disease ascariasis bilharziasis

II TOXIC

(a) Uræmia

(b) Acute febrile condition such as septicæmia pneumonia influenza measles bacterial endocarditis acute otitis media in children

(c) Pulmonary tuberculosis

(d) Poisoning by arsenic or mercury

(e) Epidemic dropsy

III NEOPLASTIC

(a) *Benign*—Rectal polyp

(b) *Malignant*—(i) Colonic or rectal carcinoma (ii) Lympho sarcoma

IV CHRONIC PORTAL CONGESTION Diarrhœa seen in cases of congestive cardiac failure cirrhosis of liver

V AMYLOID INFILTRATION Diarrhœa associated with chronic suppurative conditions

History of the Present Illness

DURATION *Short* in the acute infective and toxic diarrhœas

Long in the following types of diarrhœas

(a) Chronic amœbiasis It may persist in a quiescent state as long as forty years (*Manson Bahr*)

(b) Gastrogenous diarrhœa

(c) Nervous diarrhœa

(d) Allergic diarrhœa

(e) Tuberculous enterocolitis

MODE OF ONSET

Acute

(a) Acute infective diarrhœas

(b) Toxic diarrhœa The diarrhœas associated with pul monary tuberculosis or focal sepsis are however not characterised by an acute onset

DIAGNOSIS OF DIARRHŒAS IN THE TROPICS

Diarrhœas are so frequent in the tropics and have such a varied etiology that every general practitioner must have a clear conception of the causes of diarrhœas before he can undertake a thorough investigation for an accurate diagnosis of the underlying condition

The following classification of diarrhœas will we hope prove useful to the practitioners

A FUNCTIONAL DIARRHŒAS

I INCREASED MOTOR ACTIVITY OF THE ALIMENTARY TRACT

(a) *Dietetic*—(i) Mechanical irritation by excess of green vegetables salads and coarse raw fruits

(ii) Chemical irritation by the products of fermentation or putrefaction carbohydrates and proteins respectively

The dietetic diarrhœas are especially common in infants and children

(b) *Gastrogenous*—(i) Diarrhœa associated with gastric achylia or hypochlorhydria

(ii) Diarrhœas associated with gastro jejunostomy or partial gastrectomy

(c) *Nervous*—(i) Reflex (lienteric or post prandial) diarrhœa due to the exaggerated gastrocolic reflex

(ii) Psychical as a result of anxiety or fear

(d) *Allergic*—due to hypersensitiveness to certain articles of diet such as prawn crabs mushroom

(e) *Spurious*—caused by the irritation of scybali or habitual use of aperients

II DEFICIENT DIGESTION AND ABSORPTION OF FAT (a) Pancreatic diarrhœa (b) Diarrhœa of obstructive jaundice (c) Sprue (d) Cœliac disease

III ENDOCRINE DYSFUNCTION (a) Hyperthyroidism (Graves s disease) (b) Addison s disease

IV METABOLIC Pellagra hypoproteinæmia diabetes mellitus

B ORGANIC DIARRHŒAS

I INFECTIVE

(a) *Bacterial*—

(i) *Specific* Typhoid and paratyphoid fevers acute bacterial food poisoning cholera tuberculous enteritis

(ii) *Non specific* Acute infective diarrhœa of infants and children chronic ulcerative colitis

(*b*) *Protozoal*—Ciliate flagellate amœbic malarial leishmanial

(*c*) *Helminthic*—Hookworm disease ascariasis bilharziasis

II Toxic

(*a*) Uræmia

(*b*) Acute febrile condition such as septicæmia pneumonia influenza measles bacterial endocarditis acute otitis media in children

(*c*) Pulmonary tuberculosis

(*d*) Poisoning by arsenic or mercury

(*e*) Epidemic dropsy

III Neoplastic

(*a*) *Benign*—Rectal polyp

(*b*) *Malignant*—(i) Colonic or rectal carcinoma (ii) Lympho sarcoma

IV Chronic Portal Congestion Diarrhœa seen in cases of congestive cardiac failure cirrhosis of liver

V Amyloid Infiltration Diarrhœa associated with chronic suppurative conditions

History of the Present Illness

Duration *Short* in the acute infective and toxic diarrhœas

Long in the following types of diarrhœas

(*a*) Chronic amœbiasis It may persist in a quiescent state as long as forty years (*Manson Bahr*)

(*b*) Gastrogenous diarrhœa

(*c*) Nervous diarrhœa

(*d*) Allergic diarrhœa

(*e*) Tuberculous enterocolitis

Mode of Onset

Acute

(*a*) Acute infective diarrhœas

(*b*) Toxic diarrhœas The diarrhœas associated with pul monary tuberculosis or focal sepsis are however not characterised by an acute onset

Gradual

(*a*) Functional diarrhœas

(*b*) Chronic infective diarrhœas such as chronic amœbiasis chronic bacillary dysentery giardiasis chronic ulcerative colitis tuberculous enterocolitis

(*c*) Neoplastic diarrhœa

(*d*) Diarrhœa due to circulatory disturbances

With Abdominal Pain (*a*) Infective diarrhœas except cholera (*b*) Neoplastic diarrhœas (*c*) Diarrhœas due to dietetic errors

Without Abdominal Pain (*a*) Cholera (*b*) Sprue cœliac disease (*c*) Giardia is (*d*) Nervous diarrhœa (*e*) Allergic diarrhœa (*f*) Thyrotoxic diarrhœa (*g*) Gastrogenous diarrhœa due to gastric achylia

With Vomiting (*a*) Acute infective diarrhœa (summer diarrhœa) of children (*b*) Cholera (*c*) Bacterial food poisoning (*d*) Dietetic diarrhœas of children (*e*) Allergic diarrhœas (*f*) Toxic diarrhœas

The frequency of vomit and its relation to the diarrhœa should be noted

Appetite A good appetite is often present in

(*a*) Nervous diarrhœas (*b*) Allergic diarrhœas (*c*) Chronic amœbiasis (*d*) Chronic ulcerative colitis

FEVER Presence of fever suggests the following

With acute diarrhœas

(*a*) Acute infective diarrhœa of infants and children

(*b*) Typhoid and para typhoid fevers

(*c*) Bacterial food poisoning

(*d*) Bacillary dysentery

(*e*) Amœbic dysentery

(*f*) Pneumonia influenza measles septicæmia

(*g*) Malignant malaria

(*h*) Epidemic dropsy

With chronic diarrhœas

(*a*) Tuberculous enterocolitis

(*b*) Chronic bacillary dysentery

(*c*) Ulcerative colitis

Personal History

Careful enquiry should be made into the state of previous health and into the habits of the patient regarding excess of alcohol tobacco and tea The presence and or absence of teeth and the use of false teeth should be enquired Special enquiries are necessary on the following points

(a) Dysentery

(b) Alternating attacks of constipation and diarrhœa are suggestive of chronic amœbiasis giardiasis colonic or rectal carcinoma nervous diarrhœa

(c) Cough hæmoptysis and pleurisy are suggestive of tuberculous infection

(d) Asthma and urticaria

(e) Diabetes mellitus

(f) Nephritis

(g) Syphilitic infection

Family History

Enquiry should be made whether any of the following is present among the parents or members of the family

(a) Allergic manifestations
(b) Nervous instability
(c) Nutritional deficiencies
(d) Amœbic infection
(e) Tuberculous infection
(f) Epidemic dropsy

General Examination

NUTRITION It is fairly good in the following

Nervous allergic and gastrogenous diarhœas

EMACIATION It is indicative of

Tuberculous enterocolitis
Colonic or rectal carcinoma
Chronic bacillary dysentery
Chronic amœbiasis
Chronic ulcerative colitis (non specific)
Sprue
Cœliac disease
Pancreatic diarrhœa

ANÆMIA It occurs in helminthic infection in addition to those causing emaciation

FOCAL SEPSIS Gums teeth tonsils nasal sinuses should be carefully searched for evidences of focal sepsis which may cause diarrhœa.

Systemic Examination

ALIMENTARY SYSTEM *Tongue*

Glossitis is present in the following

Sprue	Chronic amœbiasis
Pellagra	Tropical macrocytic anæmia
Tuberculous enteritis	Chronic syphilitic infection

Abdomen It is inspected for shape movement and visible peristalsis Next it is palpated for the detection of enlargement of liver spleen gall bladder and mesenteric lymphnodes thickening of the bowel wall and omentum tenderness over cæcum appendix gall bladder and various parts of the colon The feel of the abdomen whether soft doughy or rigid is noted Examination is also made for evidence of free fluid in the peritoneal cavity

Doughy and distended abdomen indicates

Tuberculous enterocolitis and peritonitis
Sprue

Retracted abdomen occurs in

Chronic ulcerative colitis

Colonic tenderness is present in

Chronic amœbiasis
Chronic bacillary dysentery
Chronic ulcerative colitis (rarely)

RECTAL EXAMINATION In every case of chronic diarrhœa the rectum should always be examined *by the digital method* or *by the sigmoidoscope* Such an examination will often help in the diagnosis of

Hæmorrhoids
Rectal polyp
Chronic bacillary dysentery
Chronic amœbiasis
Rectal or colonic carcinoma

It must be emphasized here that the other systems such as the respiratory cardiac urinary and the nervous should receive appropriate attention in the investigation of a case of diarrhœa

Laboratory Investigation

I EXAMINATION OF THE STOOLS This is the most important part of the investigation The stools should be examined with the naked eye and also with the microscope

Macroscopic Examination

Frequency The number of stools is usually less than 6 in the following diarrhœal conditions

Dietetic diarrhœas nervous diarrhœa chronic amœbiasis chronic bacillary dysentery tuberculous enteritis sprue cœliac disease gastrogenous diarrhœa rectal or colonic carcinoma spurious diarrhœa

Quantity It is usually *copious* in sprue hill diarrhœa cœliac disease giardiasis tabes mesenterica pancreatic diarrhœa obstructive jaundice lymphadenoma and lymphosarcoma of the mesenteric lymphnodes

Colour A *pale colour* is usually found in conditions where the stools are copious *Green or greenish yellow stools* are due to an inflammation of the small intestine which hurries the bile

Smell The smell is *very offensive* in sprue obstructive jaundice and amœbiac dysentery

The stools have a *rather inoffensive smell* in cholera and bacillary dysentery

Character *Watery stools* are found in spurious diarrhœa due to purgatives cholera typhoid and paratyphoid fevers bacterial food poisoning toxic diarrhœa of pneumonia influenza growth of the small intestine tuberculous enteritis septicæmia heat hyperpyrexia and heat cramps *Unformed but non fluid stools are* seen in colonic diarrhœas

Mucus It is an index of inflammation if the stools are unformed but not so if they are scybalous The larger the flakes of mucus the lower is the site of inflammation

Mucous casts of the bowel are present in mucomembranous colic

Blood (Bright red) It is present in the following conditions (1) rectal polyp (2) hæmorrhoids (3) rectal carcinoma (4) acute bacillary dysentery in the early stage (5) chronic amœbiasis

Blood mucus and pus A combination of all these constituents is present in (1) bacillary or amœbic dysentery (2) malignant disease of the pelvic colon and rectum (3) rectal polyp (4) chronic non specific ulcerative colitis (5) diverticulitis (6) rupture of an extrinsic abscess into the intestine In the

last condition however the pus is usually separate from the stools and not intimately mixed

A careful search should be made by repeated washing and sieving of the stools for the presence of gall stones enteroliths and worms especially for the head of the tapeworm

Bio chemical Examination

Tests should be carried out to ascertain the *reaction* of the stools and to detect the presence of *bile pigment* and *occult blood* A chemical analysis of the stools for the e timation of the relative amounts of *neutral fats* and *fatty acids* and *soaps* may be necessary in differentiating pancreatic diarrhœas from those due to sprue cœliac disease jaundice and tabes mesenterica

Microscopical Examination

It is a very important method of investigation which is often helpful in the ætiological diagnosis of diarrhœas A sample of freshly passed stool after a saline purgative should be examined for the presence of ova parasites cysts (especially *E histolytica* and *Giardia intestinalis*) red blood cells pus cells mucus undigested meat fibres starch granules neutral fat fatty acid crystals and soap It should be emphasized here that the presence of Charcot Leyden crystals is not pathognomonic of amœbiasis A special search should also be made for the *Mycobacterium tuberculosis*

The microscopical examination of the mat rial remo ed from the ulcers directly through a sigmoidscope is of immense alue in such cases

Stools which yield negative results on repeated microscopical examinations are indicative of (1) sprue (2) gastrogenous diarrhœa (3) pellagra

Cultural Examination

The routine culture of stools is of limited value in the diagnosis of the diarrhœas It is however of considerable value in the bacteriologicall dliagnosis of dysentery and bacterial food poisoning

II EXAMINATION OF THE BLOOD Blood examination may be helpful in the diagnosis of diarrhœas associated with Addisonian anæmia tropical macrocytic anæmia sprue and helminthiasis A Wassermann reaction of the serum may be done in obscure cases of diarrhœa

III FRACTIONAL TEST MEAL Gastric achlorhydria or hype

chlorhydria is present in pellagra sprue tropical macrocytic anæmia and Addisonian anæmia

Radiological Examination

X ray *examination of the alimentary* tract with the barium meal or enema is particularly useful in the diagnosis of gastrogenous diarrhœa colonic diarrhœas due to carcinoma and diverticulitis The characteristic radiological appearance of sprue intestine is helpful in diagnosis Radiological examination of the chest may be necessary in obscure cases

Lastly we would point out that the cause of a large number of cases of diarrhœa may remain obscure in spite of a thorough investigation In such cases the possibility of nervous gastrogenous and allergic diarrhœas should be kept in mind

THERAPEUTIC GUIDE

ANÆMIA (HYPOCHROMIC)

R/

Ferri et Ammonii Citratis	dr ½
Glycerini	dr ½
Syrupi Aurantii	dr ½
Aquæ ad	oz i

Fiat mistura

Sig One dose three times a day one hour after meals

ANGINA PECTORIS (EFFORT ANGINA)

R/

Tabellæ Glycerylis Trinitratis	gr 1/100

Sig One tablet is to be *chewed* and then swallowed

It is indicated for the relief of the cardiac pain Between the attacks the associated cardiovascular condition should receive appropriate treatment

ANOREXIA

Sodii Bicarbonatis	gr xv
Tincturæ Nucis Vomicæ	m v
Infusi Gentianæ Compositæ	dr ii
Aquæ ad	oz i

Fiat mistura

Sig One dose three time a day half an hour before meals

ARTHRITIS (ACUTE RHEUMATISM)

R/

Sodii Salicylatis	gr xx
Sodii Bicarbonatis	gr xv
Glycerini	dr ½
Syrupi Aurantii	dr i
Aquæ ad	oz i

Fiat mistura

Sig One dose every three to four hours with an equal quantity of water till the temperature comes down and the joint pains subside Subsequently one dose every six hours for a few weeks will suffice

ASCARIASIS

(See page 153)

R/

Santonini	gr iii
Hydrargyri Subchloridi	gr ii

Fiat pulvis

Sig To be taken at bed time followed by a dose of saline purgative early next morning

ASTHMA

R/

Potasii Iodidi	gr v
Potassii Bromidi	gr x
Ephedrinæ Hydrochloridi	gr ½
Tincturæ Stramonii	m xv
Spiritus Chloroformi	m xx
Aquæ Menthæ Piperitæ ad	oz i

Fiat mistura

Sig One dose every six hours after meals During the *acute attack* ½ c cm of adrenaline hydrochloride 1 in 1000 or gr 1/100 of atropine sulphate should be injected hypodermically Specific desensitisation should be tried whenever possible

BACILLURIA

(*Esch coli infection*)

R/

Potassii Citratis	gr xx
Sodii Bicarbonatis	gr xx
Syrupi Aurantii	dr i
Aquæ ad	oz i

Fiat mistura

Sig One dose every 4 hours The urine is to be *kept alkaline for a period of 7 days* Administration of sulphadiazine tablets in dose of 1 g

6 hourly till the temperature is normal and subsequently 0.5 g 8 hourly for 3-5 days. Streptomycin intramuscularly—1.2 g daily for 4-5 days.

BRONCHIECTASIS

R/

Potassii Iodidi	gr v
Ammonii Carbonati	gr v
Olei Creosoti	m iii
Mucilaginis Acaciæ	dr ii
Syrupi Tolutani	dr ½
Aquæ Menthæ Piperitæ ad	oz i

Fiat mistura

Sig. One dose is to be taken thrice daily after meals to promote expectoration and to reduce the fetor of the sputum. *Postural drainage is essential to empty the bronchiectatic cavities.*

BRONCHITIS (ACUTE)

(Dry stage)

R/

Tincturæ Benzoini Compositæ	oz i

Sig. One teaspoonful is to be added to a pint of boiling water in a steam kettle and the vapour to be inhaled for 10 minutes. The patient must however be confined to bed.

R/

Potassii Acetatis	dr ½
Tincturæ Ipecacuanhæ	m x
Syrupi Tolutani	dr ½
Aquæ ad	oz i

Fiat mistura

Sig. One dose every three hours.

(Stage of scanty secretion)

R/

Ammonii Carbonatis	gr v
Tincturæ Ipecacuanhæ	m x
Syrupi Tolutani	dr ½

Fiat mistura

Sig. One dose three times a day.

BRONCHITIS (CHRONIC)

Sodii Bicarbonati	gr x
Sodii Chloridi	gr ii
Spiritus Chloroformi	m v
Aquæ Anisi ad	oz i

Fiat mistura

Sig. One dose is to be taken with an equal quantity of warm water in the morning and evening. *(Brompton Hospital Pharmacopœia)*

R/

Potassii Iodidi	gr v
Potassii Bicarbonatis	gr x
Ammonii Carbonatis	gr v
Tincturæ Ipecacuanhæ	m x
Syrupi Tolutani	dr i
Aquæ Chloroformi ad	oz i

Fiat mistura

Sig. One dose three times a day. Indicated when the sputum is viscid and scanty.

CHOLECYSTITIS (ACUTE)

R/

Potassii Citrati	dr
Hexaminæ	gr xv
Syrupi Aurantii	dr i
Aquæ ad	oz i

Fiat mistura

Sig. One dose every 4 hours. Urine should be *kept on to the alkaline* to avoid irritation of the urinary bladder.

COLLAPSE (FAINTING)

R/

Spiritus Ammoniæ Aromaticæ	dr i
Spiritus Ætheris	m xx
Spiritus Chloroformi	m xx
Aquæ Cinnamomi ad	oz i

Fiat mistura

Sig. One dose is to be taken immediately. It is an efficient reflex vasomotor stimulant.

Colic (Intestinal)

Potassii Bromidi	gr	x
Tincturæ Belladonnæ	m.	v
Spiritus Chloroformi	m	xv
Aquæ Menthæ Piperitæ ad	oz	½

Fiat mistura

Sig One dose every 4 hours

Conjunctivitis (Acute)

R/

Sodii Chloridi	gr	xviii
Aquæ Destillatæ	oz	iv

Fiat lotio

Sig The affected eye should be irrigated with this solution The eye lids should be smeared with a 2% boric acid ointment

Conjunctivitis (Chronic)

R/

Zinci Sulphatis	gr	i
Aquæ Destillatæ	oz	i

Fiat guttæ

Sig To drop into the affected eye

R/

Argyroli	dr	1½
Aquæ Destillatæ	oz	i

Fiat guttæ

Sig To instil a few drops into the affected eye The lids should be smeared at night by one half per cent ointment of the yellow oxide of mercury

Constipation (Habitual)

R/

Extracti Cascaræ Sagradæ Sicci	gr	iii
Extracti Nucis Vomicæ Sicci	gr	¼
Extracti Belladonnæ Sicci	gr	¼

Fiat pilula

Sig One pill at bed time useful in colonic constipation *Re-establishment of the normal defæcation reflex is essential*

Corneal Ulcer

R/

Iodoformi	gr	ix
Atropinæ Sulphatis	gr	iv
Paraffini Mollis	oz	i

Fiat unguentum

Sig To be applied to the eye lid of the affected side after irrigation with normal saline Hot compresses and instillation of a few drops of a 2 per cent. solution of protargol are also resorted to

Cough (Non productive)

R/

Diamorphinæ Hydrochloridi	gr	⅛
Syrupi Tolutani	m	xx
Syrupi Pruni Serotinæ	m	xx
Glycerini ad	dr	i

Fiat linctus

Sig One dose is to be taken if the cough is severe

R/

Liquoris Morphinæ Hydrochloridi	m	xx
Acidi Hydrocyanici Diluti	m	iii
Syrupi Pruni Serotinæ	m	xx
Glycerini ad	dr	i

Fiat linctus

Sig One dose to be licked slowly in case of severe irritating cough

R/

Syrupi Codeinæ Phosphatis	dr	ii
Spiritus Chloroformi	m	xx
Glycerini	m	xx
Syrupi Tolutani ad	oz	½

Fiat linctus

Sig One dose to be licked slowly

Diarrhœa (Acute)

R/

Bismuthi Carbonati	dr	½
Cretæ	gr	xx
Tincturæ Catechu	m.	xx
Syrupi Zingiberis	dr	½
Pulveri Tragacanthæ Co	gr	v
Aquæ Cinnamomi ad	oz	i

Fiat mistura

Sig One dose every four hours. Regulation of the diet with treatment of the underlying cause is essential.

DROPSY (CARDIAC)

R/

Potass. Acetatis	dr	½
Theophyllinæ et Sodii Acetatis ..	gr	ii
Tincturæ Scillæ	m	x
Aquæ Menthæ Piperitæ ad	oz	i

Fiat mistura

Sig One dose every six hours for four consecutive days in the week.

R/

Pilulæ Hydrargyri	gr	v

Sig One pill at bed time followed by an ounce of saturated solution of magnesium sulphate in the morning.

R/

Tincture Digitalis (B.P.)	oz	i

Sig Twenty minims to be taken in half an ounce of water every six hours till the pulse rate is slowed down to 80 per minute or a coupling of the beats occurs.

R/

Pulveris Foliæ Digitalis	aa gr	i
Pulveris Scillæ		
Pilulæ Hydrargyri		

Fiat pilula

Sig One pill three times a day after meal. This is known as *Guy's pill*.

In obstinate cases of cardiac dropsy intramuscular injection of 1-2 c.cm. of mercurials supplemented with the oral administration of gr. 90 of ammonium chloride a day is very useful. Diamox or di-chlorothiazide is also very effective.

DROPSY (RENAL)

R/

Potassii Acetatis	gr	xx
Potassii Citratis	gr	xx
Syrupi Aurantii	dr	i
Aquæ ad	oz	i

Fiat mistura

Sig One dose every six hours. A moderately high protein diet calculated on the basis of 1 g. of protein per pound of the expected body weight in absence of any retention of the non-protein nitrogenous constituent of the blood is very helpful.

R/

Potassii Acetatis	gr	xx
Liquoris Ferri Acetatis	m	x
Liquoris Ammonii Acetatis (Diluti)	dr	ii
Aquæ Chloroformi ad	oz	i

Fiat mistura

Sig One dose to be taken four times a day after meals. (*Basham's mixture*)

DYSENTERY (AMOEBIC)

(See page 5)

DYSENTERY (BACILLARY)

(See page 232)

DYSPEPSIA (HYPOCHLORHYDRIC)

R/

Acidi Hydrochlorici Diluti	m	xx
Liquoris Strychninæ Hydrochlorid ..	m	v
Spiritus Chloroformi	m	xx
Infusi Gentianæ Compositæ ad	oz	i

Fiat mistura

Sig One dose to be taken diluted with an equal quantity of water thrice daily one hour after meal.

DYSURIA (CYSTITI[illegible])

R/

Potassii Bromidi	gr	x
Potassii Citratis ..	dr	½
Tincturæ Hyoscyami ..	m	xx
Aquæ Chloroformi ad ..	oz	i

Fiat mistura
Sig One dose thrice daily

EARACHE (FURUNCULOSIS)

R/

Ichthyolis ..	gr xiv
Glycerini ..	oz i

Fiat guttæ

Sig A wick of cotton soaked in drops to be inserted into the meatus only a day Hot fomentations with bran bags are useful

EARACHE (ACUTE OTITIS MEDIA)

R/

Glycerini Acidi Carbolici (B P)	dr ii
Glycerini ad	oz i

Fiat guttæ

Sig To be warmed and instilled into the ear four hourly

EARACHE (CHRONIC OTITIS MEDIA)

R/

Liquidi Acidi Carbolici	m v
Spiritus Vini Recti	oz ½
Aquæ Destillatæ	oz ½

Fiat guttæ

Sig A few drops to be instilled into the affected ear after it has been *thoroughly mopped dry* It should then be kept uppermost for 5 minutes Excess of the drops should be dried out and the ear *left open*

ECZEMA

R/

Phenolis	gr xx
Lotio Calaminæ	oz iv

Fiat lotio

Sig To be applied over the affected parts Indicated in presence of erythema and itching

R/

Hydrargyri Ammoniati	gr x
Zinci Oxidi	gr xv
Liquoris Picis Carbonis ...	dr i
Vaselini ..	oz i

Fiat unguentum

Sig To apply over the affected parts Indicated in chronic cases

EPILEPSY (IDIOPATHIC)

R/

Luminalis	gr ½
Lactosi	gr v

Fiat pulvis

Sig One dose i to be taken in the morning If necessary the dose of luminal may gradually be increased to one grain and a half a day

The treatment should be continued for two years

Dilantin sodium (Phenytoinum sodium) is useful for cases of grand mal not responding to luminal The dose for adults is gr 1½ thrice daily Change of therapy from luminal to dilantin should be gradual with overlapping of dosage

Tridione is valuable in petit mal and myoclonic and akinetic epilepsy It is supplied in 0 3 g capsule Dose—1 capsule 3 to 4 times a day

ENTEROBIASIS

(See page 158)

FEVER

R/

Potassii Citratis	gr xx
Potassii Acetatis	gr xx
Syrupi Aurantii	dr i
Aquæ Menthæ Piperitæ ad	oz i

Fiat mistura

Sig One dose to be taken at six hourly interval to promote heat loss by diaphoresis and diuresis

FLATULENCE

R/

Magnesii Carbonatis Ponderosi	gr x
Spiritus Menthæ Piperitæ	m v

Spiritus Chloroformi	m. xv
Syrupi Zingiberis	dr ½
Aquæ Anethi ad	oz 1

Fiat mistura

Sig One dose to be taken when required

R/

Menthol s	gr iv
Spiritus Ammoniæ Aromaticæ	dr 1
Spiritus Chloroformi	oz 1

Fiat mistura

Sig One teaspoonful to be taken with water when required

GIARDIASIS

(See page 38)

GOUT

R/

Potassii Iodidi	gr x
Sodii Salicylatis	gr xv
Sodii Bicarbonatis	dr ½
Tincturæ Colchici	m xv
Spiritus Chloroformi	m xv
Aquæ ad	oz 1

Fiat mistura

Sig One dose to be taken diluted with an equal quantity of water thrice daily after meals

HICCOUGH (PERSISTENT)

Potassii Bromidi	gr x
Chloral Hydratis	gr x
Tincturæ Belladonnæ	m. x
Spiritus Chloroformi	m xx
Aquæ Menthæ Piperitæ ad	oz 1

Fiat mistura

Sig One dose every three hours until three doses are given

Oral octyl nitrite and largactil are effective Inhalation of carbon dioxide may be helpful Treatment of the underlying cause is essential.

HOOKWORM DISEASE

(See page 141)

IMPETIGO

R/

Hydrargyri Ammoniati	gr x
Paraffini Mollis	oz 1

Fiat unguentum

Sig To apply over the affected parts after removal of the crusts by warm baths and hot fomentations

INFLUENZA

R/

Potass Bromidi	gr xv
Sodii Bicarbonatis	gr xx
Sodii Salicylatis	gr x
Syrupi Aurantii	dr 1
Aquæ ad	oz 1

Fiat mistura

Sig One dose four times a day

R/

Acidi Acetylsalicylici	gr v
Phenacetini	gr v
Caffeinæ Citratis	gr iii

Fiat pulvis

Sig One powder to be taken every four hours for the relief of headache and muscular pains

R/

Mentholi	gr x
Spiritus Vini Recti	oz 1

Fiat inhalatio

Sig To put 20 drops into a pint of boiling water and inhale the vapour for the relief of tracheo-bronchitis

INSOMNIA

R/

Potas Bromidi	gr xx
Chloralamidi	gr xx
Alcoholis	m xx
Syrupi Aurantii	dr 1
Aquæ ad	oz 1

Fiat haustus

Sig One dose to be taken at bed

time Indicated in insomnia associated with cardiovascular di ease or mental worry

INFECTIOUS JAUNDICE (VIRAL)

R/

Pilulæ Hydrargyri	gr v

Sig One pill at bed time followed by an ounce of saturated solution of magnesium sulphate early in the morning

To be continued for a few weeks

R/

Sodii Bicarbonatis	gr xx
Sodii Citratis	dr ½
Hexaminæ	gr xx
Aquæ ad	oz 1

Fiat mistura

Sig One do e to be taken every 3 hours The urine should be *kept alkaline* to prevent irritation of the urinary bladder

LARYNGITIS (ACUTE)

R/

Olei Pini Sylvestris	m xl
Magnesii Carbonatis Levi	dr ½
Aquæ ad ..	oz 1

Fiat inhalatio

Sig One teaspoonful to be added to a pint of boiling water and the vapour inhaled *Voice-rest is essential*

R/

Mentholis	gr v
Chloretoni	gr v
Paraffini Liquidi	oz 1

Fiat nebula

Sig To spray into the larynx in *subacute laryngitis*

LUMBAGO (ACUTE)

Acidi Acetylsalicylici ..	gr x
Phenacetini	gr v
Caffeinæ Citratis	gr ii

Fiat pulvis

Sig One dose four times a day Application of dry hot fomentations and massage is essential Applications of *infra red* are useful

MALARIA

(See page 40)

R/

Quininæ Dihydrochloridi	gr vii
Aquæ Chloroformi	oz ½

Fiat mistura

Sig One dose thrice daily for a week An alkalinising mixture should be given half an hour previous to the quinine mixture

R/

Quininæ Dihydrochloridi	gr x
Aquæ Destillatæ	dr ½

Fiat injectio

Sig Inject intramuscularly if urgent cerebral symptoms or signs of gastro-intestinal irritation are present.

No 1

R/

Quininæ Sulphatis ..	gr vii
Acidi Citrici	gr xv
Aquæ Chloroformi	oz ½

No 2

R/

Potassii Bicarbonatis	gr xv
Syrupi Aurantii	dr ½
Aquæ ad	oz ½

Sig One dose of No 1 to be mixed with one dose No 2 and taken while effervescing three times a day (*Effervescent Quinine Mixture*)

R/

Cinchonæ Febrifugis	gr x
Acidi Citrici ..	gr xx
Spiritus Chloroformi	m xx
Aquæ ad ...	oz 1

Fiat mistura

Sig One do e three times a day a week 3 hours after meals Indicated

for its cheapness combined with efficacy

R/

Ferri Sulphatis	gr v
Quininæ Sulphatis	gr v
Sodii Sulphatis	gr xx
Liquoris Arsenicalis	m iii
Acid Sulphuri i Diluti	m x
Aquæ Menthæ Piperitæ ad	oz i

Fiat mistura

Sig One dose to be taken thrice daily after meals for a week. Indicated in *chronic malaria*

MIGRAINE

R/

Luminalis	gr ½
Potassii Bromidi	gr x

Fiat pulvis

Sig One powder to be taken twice a day

R/

Ergotamine Tartrati	gr 1/100
Aquæ Destillatæ	dr ½

Fiat injectio

Sig To be injected hypodermically during the attack

This is a successful method of relieving the migramous headache

Removal of allergic factors wherever possible is necessary

NEURASTHENIA

R/

Ferri Sulphatis	gr v
Liquoris Strychninæ Hydrochloridi	m v
Acidi Phosphorici Diluti	m xx
Syrupi Chloroi	dr i
Aquæ Chloroformi ad	oz i

Fiat mistura

Sig One dose thrice daily after meals

NEURITIS (SCIATICA)

R/

Linimenti Aconiti	oz i
Linimenti Belladonnæ	oz ii
Linimenti Chloroformi	oz ii

Fiat linimentum

Sig Half an ounce of the liniment to be painted twice daily over the affected region after dry hot fomentation or preferably after exposure to infra-red rays from a portable lamp for half an hour. The part should then be wrapped up in cotton wool. A P C gr x may be used to relieve the pain

ORCHITIS

R/

Ichthyoli	dr v
Extracti Belladonnæ Viridi	dr iv
Glycerini ad	oz i

Fiat pigmentum

Sig To apply locally over the affected site

PEPTIC ULCER

R/

Bismuthi Carbonati	gr xxv
Magnesii Carbonatis Ponderosi	gr xv
Cretæ	gr xx

Fiat pulvis

Sig One fraction to be taken half an hour after each meal to control the free acidity. The patient should however be put under a modified Sippy's diet.

Magnesium trisilicate in one drachm dose taken half an hour after each meal is a very good antacid

R/

Tincturæ Belladonnæ	m x
Spiritus Chloroformi	m x
Aquæ ad	oz ½

Fiat mistura

Sig One dose three times a day half an hour before each meal It is useful in controlling the pylorospasm and the hyperchlorhydria

Pertussis

R/

Potassii Bromidi	gr	ii
Chloralis Hydratis	gr	i
Tincturæ Belladonnæ	m	iii
Syrupi Aurantii	m	xx
Aquæ Anethi ad	dr	i

Fiat mistura

Sig One dose to be given every six hours to a child of 2 years The dose of the tincture of belladonna may be pushed to its physiological limit

Pharyngitis

Same as in Tonsillitis

Pruritus

Application of one per cent phenolized calamine lotion is very useful A careful search should be made to find out the underlying cause

Rhinitis

R/

Sodii Bicarbonatis Sodii Biborati Sodii Chloridi	aa gr	xv
Phenolis Liquefacti	m	iii
Glycerini	dr	vi
Aquæ ad	oz	vi

Fiat lotio

Sig To irrigate the nasal cavities with a small glass nasal douche

Ringworm

R/

Acidi Salicylici	gr	xv
Acidi Benzoici	gr	xxii
Paraffini Mollis	oz	i

Fiat unguentum

Sig To rub over the affected parts twice a day for ten days

Scabies

R/

Sulphuris Sublimati	dr	i
Paraffini Mollis	oz	i

Fiat unguentum

Sig The ointment is rubbed in all over the body (except the face and scalp) after soaking the whole body in hot water for about 15 minutes rubbing with soft soap then scrubbing especially the affected parts with a stiff nail brush or a rough towel and finally drying it The patient puts on disinfected clothes The application is continued for two more days without any bath On the fifth day a bath is taken to remove the sulphur ointment and the clothes are changed All dirty under clothing is boiled

R/

Benzylbenzoatis	oz	1½
Linimenti Saponis Mollis	oz	ii
Alcoholis (90%)	oz	ii
Aquæ Destillatæ	dr	1½

(After Kissmeyer & Goldman)

Fiat lotio

Sig After bath in the way described above the wet body is brushed all over with the lotion for five minutes and allowed to dry The lotion is again applied in the same way for another five minutes and after drying clean clothes are put on A second bath is taken 24 hours later and the clothes are changed

Stomatitis

R/

Potassii Chloratis	gr	x
Acidi Hydrochlorici Diluti	m	x
Syrupi Limonis	dr	i
Aquæ ad	oz	i

Fiat mistura

Sig One dose thrice daily for 3-4 days

R/
Potassii Chlorati ... dr ii
Acidi Hydrochlorici (Puri) m x
Glycerini dr iv
Aquæ ad oz viii

Fiat gargarisma

Sig Half an ounce to be mixed in a cup of water and used for gargling

SYPHILIS (TERTIARY)

R/
Potassii Iodidi gr x
Liquoris Hydrargyri Perchlorid dr i
Spiritus Chloroform m xx
Aquæ ad oz

Fiat mistura

Sig One dose to be taken thrice daily for a period of six weeks prior to the commencement of treatment with an arsenical compound The dose of iodid may be gradually increased to gr 90 a day

R/
Hydrargyri cum Cretæ
Pulveris Ipecacuanhæ Composite aa gr i

Fiat pulvis

Sig One powder to be taken twice daily Attention should be paid to the teeth and gums

Penicillin 600 000 units daily for two weeks

TENIASIS

(See page 167)

TONSILLITIS (ACUTE)

R/
Resorcinol gr xl
Phenolis Liquefact ... m x
Spiritus Menthæ Piperitæ m xv
Glycerini ad ... oz i

Fiat pigmentum

Sig To paint inside the throat thrice daily

A sodium salicylate mixture may be given Administration of sulphadiazine tablets in doses of 2 tablets (0 5 g each) six hourly is also useful

R/
Sodii Bicarbonati dr ½
Sodii Chloridi dr ½
Potassii Chlorati dr i
Phenolis Liquefacti m v
Aquæ ad oz viii

Fiat lotio

Sig Warm the lotion and syringe inside the throat every 4 hours

A very useful measure

TONSILLITIS (CHRONIC)

R/
Iod gr vi
Potass Iodid gr xv
Phenolis Liquefact m x
Olei Menthæ Piperitæ m i
Glycerini ad oz i

Fiat pigmentum

Sig To paint inside the throat thrice daily

URTICARIA

R/
Calcii Gluconatis gr x
Ephedrinæ Hydrochloridi gr ½

Fiat pulvis

Sig One powder to be taken twice a day for a week Antihistaminics oral or injectable During a severe attack ½ c cm of adrenaline hydrochloride 1 in 1000 should be injected intramuscularly The source of allergy should be investigated

WAX (EAR)

R/
Sodii Bicarbonatis dr ½
Aquæ Destillatæ ... oz i

Fiat guttæ

Sig To instil into the affected ear four hourly for a day after which the ear should be syringed with warm boric lotion

SUBJECT INDEX

D

DRUG INDEX

V

Y

P blish d by B Dh 11 P ha Ghosh La C lcutta 9 d p t d by Trid b h B B A. t K P B Pri t g W rks, 11 M h d Go sain La Calcutta 6

V

Y

P blish d by B Dh 11 P hana Ghosh La C lcutta 9 and p t d by T d b h B B A t K P B P t g W ks, 11 M h d Gossai La C lcutta 6